UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

December 5, 2000

MEMORANDUM

SUBJECT: DIAZINON. Revised HED Human Health Risk Assessment for the Reregistration Eligibility Decision (RED) D270838. PC Code: 057801. List A Case No. 0238.

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This memorandum, the accompanying human health risk assessment and attachments serve as the Revised HED Human Health Risk Assessment for the RED for diazinon. This document reflects revisions to the Diazinon Preliminary Risk Assessment (4/12/00) made in response to the registrant's (Novartis) comments made during Phase 3 of the TRAC pilot process. The attachments include: 1)Report of the Hazard Identification Assessment Review Committee (HIARC) memorandum (HED Doc 014390, 11/30/00) (Attachment I), 2) HED Product Residue Chemistry Chapter dated 12/1/00(Attachment II), 3) the acute and chronic dietary exposure analyses dated 11/14/00 (Attachment III), 4) HED Occupational and Residential Exposure Assessment Chapter for Diazinon dated 11/30/00 (Attachment IV), 5) EFED Memorandum from R. D. Jones to D.Drew (dated 11/14/00) (Attachment V).

These attachments contain updated information used in this revision of the diazinon risk assessment (12/00). Cumulative risk assessment, which considers risks from other pesticides which have a common mechanism of toxicity is not addressed in this document.

Under the toxicity sections of this document, revisions have been made in response to the 60-day comment period where applicable.

Under the residue chemistry sections of this document, revisions have been made in response to the 60-day comment period. HED notes that the following raw agricultural commodities were excluded from the current dietary risk assessments: olives, peanuts, pecans, soybeans, sugarcane, beans, guar, and cowpeas. The registrant voluntarily canceled these uses on December 27, 1996. The Agency is proposing to revoke these tolerances. Secondary residues of diazinon from sheep commodities based on the sheep spray use were included as were anticipated residues in beef fat as a result of cattle ear tag use. The registrant (Novartis) has expressed interest in supporting uses on kiwi fruits, and provided the necessary residue data. IR-4 has expressed interest in supporting uses on figs, watercress, and filberts, and provided the necessary residue data for watercress and figs. These four commodities were included in the dietary risk assessment. Also included in the dietary assessments because they have tolerances were: bananas, citrus, coffee, cotton seed meal and oil, dandelion, and sorghum. The HED Residue Chemistry chapter recommends for revocation of these tolerances because the registrant no longer wishes to support these uses. SRRD has requested that these commodities be included in the dietary assessment until it has been determined that no other interested parties wish to support these uses. Once USDA, IR-4, growers groups, and others have had the opportunity to review the document, a decision can be made regarding the tolerances listed for revocation.

Under occupational/residential sections of this document, revisions have been made in response to the 60-day public comment period. The occupational/residential exposure and risk estimates have been revised to incorporate data included in new chemical specific exposure studies. A risk assessment for dermal exposures to diazinon on pet collar products was performed.

HUMAN HEALTH RISK ASSESSMENT

DIAZINON

December 5, 2000

Reregistration Branch 3
Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency

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ATTACHMENTS:

ATTACHMENT I - Hazard Identification Assessment Review Committee (HIARC) Report (HED doc 014390, 11/30/00)

ATTACHMENT II - HED Product and Residue Chemistry Chapter (D270422,dated 12/1/2000)

ATTACHMENT III - Diazinon: Acute and Chronic Dietary Risk Assessment (D269781, dated 11/14/00)

ATTACHMENT IV - HED Occupational/Residential Exposure Assessment Chapter (D270837, dated 11/30/00)

ATTACHMENT V - EFED Memorandum from R. D. Jones to D.Drew (dated 11/14/00)

EXECUTIVE SUMMARY

Introduction

Diazinon [O,O-diethyl-O-(2-isopropyl-6-methyl-4-pyrimidinyl)phosphorothioate] is a nonsystemic organophosphate insecticide/acaracide registered for use on a variety of terrestrial foods and an aquatic food (watercress), livestock feeds, and livestock (sheep sprays and cattle ear tags). Since August 1986, label statements prohibiting applications to food crops grown in greenhouses have been required. It has registered non-food uses, as well, including: food/feed handling establishments, livestock areas, and indoor/outdoor residential sites. Diazinon has veterinary uses for fleas and ticks. Currently approved veterinary uses are for impregnating pet collars with diazinon. It is available in dust, granules, seed dressings, wettable powders, and emulsifiable solution formulations. It can be applied foliarly or as a soil treatment using ground or aerial equipment followed by incorporation in most uses. Based on available usage information, for 1987 through 1997, total annual domestic usage of diazinon is approximately 13 million pounds active ingredient. Most of this is allocated to outdoor residential uses, lawn care operators, and pest control operators. States with significant usage include California, Texas, and Florida.

This document contains the results of several human health risk assessments for diazinon based on its current use patterns. All of the risk assessments included in this document were based on a common toxicological endpoint (cholinesterase inhibition) observed following oral, dermal, and inhalation exposures. For the purposes of the risk assessments conducted here, the toxicity of diazinon's oxon and hydroxy diazinon (metabolites) will be considered equivalent to the parent compound.

The general public (nonoccupational exposures) is potentially exposed to diazinon through food, drinking water, and residential uses (home, garden, and pet uses). Diazinon has a wide variety of homeowner uses including lawn treatments, spot treatments, and indoor crack and crevice treatments. Diazinon is applied outdoors by many methods including spray equipment, and granular spreaders.

Registered homeowner uses of diazinon may result in short-term dermal, inhalation (any time period), and short-term, inadvertent, oral hand-to-mouth residential exposures. Aggregate risk assessments for non-occupational exposures to diazinon have been conducted for short-term exposures.

The acute aggregate risk assessment examines 1-day exposures to diazinon in food and drinking water. The short-term aggregate risk assessment consists of average exposures to diazinon in food and drinking water, and exposures of a few days duration as a result of residential uses. The chronic aggregate risk assessment examines long-term average exposures to diazinon in food and in drinking water. There are no chronic residential exposure scenarios.

Risk assessments for occupational uses of diazinon include: short-, intermediate-, and long-term dermal and inhalation exposures. Occupational workers are potentially exposed to diazinon from a multitude of application techniques and multiple formulations. Diazinon treatments include: aerial applications, airblast, groundboom, tractor and push-type granular spreaders, and handled spray equipment.

Occupational dermal exposures of a short duration (1 to 7 days) and of an intermediate duration (7 days to several weeks) may occur. There are some potential long-term occupational exposures expected to occur from the registered uses of diazinon. However, risk estimates for these scenarios are adequately addressed by risk estimates for intermediate-term exposure scenarios because the intermediate- and chronic-term risk assessments use the same toxicological endpoint. Postapplication worker exposure may occur dermally, but not through inhalation.

Because of its widespread use in residences, diazinon is often involved in unintentional exposures. About 4% of all pesticide-related calls (estimated at 4,700 annually out of 116,000) received by the poison control centers are related to diazinon. The overwhelming majority of cases experience only minor symptoms, but about 150 cases per year are serious enough to require special medical attention. Although only a small proportion of cases involve products used by pest control operators, these exposures often involve exposures to concentrated chemical, which can lead to more serious health effects.

Hazard Assessment

The toxicology profile demonstrates that diazinon, like other organophosphate pesticides, has anticholinesterase activity in various species including hens, mice, rats, rabbits, and dogs. Clinical signs of toxicity observed in laboratory animals following an acute (single) exposure are consistent with cholinesterase inhibition and include: tremors, convulsions, salivation, and dyspnea (labored breathing). Inhibition of plasma, erythrocyte and/or brain cholinesterase (ChE) activity occurs by all routes (oral, dermal, and inhalation) and for all durations of exposure. Diazinon did not induce organophosphate delayed neuropathy (OPIDN) in hens. No histopathological lesions of the nervous system were seen in either the acute or subchronic neurotoxicity studies. In subchronic and chronic toxicity studies conducted in mice, rats and dogs, systemic toxicity was manifested as cholinergic signs, decreases in body weight and body weight gains. Diazinon is classified as a "not likely human carcinogen" based on the lack of evidence of carcinogenicity in mice and rats when tested at doses that were adequate to assess the carcinogenic potential of this organophosphate. Diazinon was shown to be non-mutagenic following both *in vivo* and *in vitro* mutagenicity assays. Prenatal developmental toxicity studies in rats and rabbits provided no evidence of increased susceptibility of rat or rabbit fetuses following *in utero* exposure. In the two-generation reproductive toxicity study, there was no evidence of increased susceptibility in the offspring as compared to parental animals. In the prenatal developmental toxicity studies, no developmental toxicity was seen at the highest dose tested, and in the two-generation reproductive toxicity study, effects in the offspring were observed only at a dose that caused parental toxicity. There was no evidence of abnormalities in the development of the fetal nervous system in these studies. Metabolism studies in rats showed that most of the administered diazinon is degraded and/or eliminated within 24 hours postdosing, and does not accumulate in tissues. Diazinon is metabolized in rats through cleavage at the ester linkage resulting in the liberation of the pyrimidinyl group that is oxidized and excreted. There were no major sex- or dose-related differences in the disposition or metabolism of diazinon.

For diazinon, the 10x Food Quality Protection Act (FQPA) safety factor, for the protection of infants and children (as required by the Food Quality Protection Act of 1996), was reduced to 1x based on the: 1) completeness of the toxicology database; 2) lack of evidence of increased susceptibility following pre-, and post-natal exposures; and 3) the use of adequate data (actual, surrogate and/or modeling outputs) to satisfactorily assess dietary and non-dietary exposures. Additionally, there was no evidence for requiring a developmental neurotoxicity study. However, the Agency, recently, has issued a Data-Call-In notice for a developmental neurotoxicity study for all organophosphates, which includes diazinon. As per current policy, a Reference Dose (RfD) modified by an FQPA safety factor is referred to as a Population Adjusted Dose (PAD). Because the FQPA safety factor was reduced to 1x, the acute and chronic RfDs are equal to the acute and chronic PADs, respectively.

For the acute dietary exposure and risk assessment, the dose selected was the No Observed Adverse Effect Level (NOAEL) of 0.25 mg/kg/day based on plasma cholinesterase inhibition at the Lowest Observed Adverse Effect Level (LOAEL) of 2.5 mg/kg/day established in an acute neurotoxicity study in rats. An Uncertainty Factor (UF) of 100 was applied to the NOAEL to account for intra-species extrapolation (10x) and inter-species variation (10x). The resultant acute RfD of 0.0025 mg/kg/day is equivalent to the acute PAD.

For the chronic dietary exposure risk assessment, the dose selected was the NOAEL of 0.02 mg/kg/day based on a weight of evidence of plasma cholinesterase inhibition (red blood cell and/or brain inhibition at higher doses) observed in a four week, subchronic and chronic (oral) studies in rats and dogs. An Uncertainty Factor (UF) of 100 was applied to the NOAEL selected to account for intra-species extrapolation (10x) and inter-species variation (10x). The resultant chronic RfD of 0.0002 mg/kg/day is equivalent to the chronic PAD.

For the short-, intermediate, and long-term dermal exposure risk assessments the dose level selected was the NOAEL of 1.0 mg/kg/day based on serum and brain cholinesterase inhibition observed at 5 mg/kg/day in a repeated dose dermal toxicity study in rabbits. For short-term occupational and residential exposure risks, a Margin of Exposure (MOE) of 100 is adequate. However, for intermediate, and long-term exposure risks, a MOE of 300 is required. since the duration of treatment in the 21-day study may not be adequate to address the concern for longer term exposures. In the previous risk assessments, dermal risk assessments were conducted using an oral NOAEL with the default dermal absorption factor (100%). Data submitted since then does not support the assumption of this default value. In addition, further analysis of the dermal toxicity study showed that this study is appropriate for use since adequate dermal absorption was demonstrated which in turn resulted in toxicity. The principal toxicological effect (i.e., cholinesterase inhibition) of this organophosphate was via the exposure route of concern (dermal), and therefore the dose endpoint of concern is obtained from a route-specific study.

For inhalation exposure (short-, intermediate-, and long-term), the dose selected was a LOAEL of 0.026 mg/kg/day (0.1 ug/L) based on inhibition of plasma cholinesterase established in a 21-day inhalation toxicity study in rats. A MOE of 300 or greater does not exceed HED's level of concern for inhalation exposure risk assessments, which includes the conventional 100x, and an additional 3x uncertainty factor for the use of a LOAEL (i.e., a NOAEL was not established in the critical study). In the case of inhalation exposures, a 100% absorption factor is assumed, therefore, the inhalation dose is equivalent to the oral dose.

Risk Characterization

Dietary Risk Estimate (Food)

The acute dietary exposure analysis estimates the distribution of single-day exposures for the overall U.S. population and certain subgroups. The exposure analysis was performed using the Dietary Exposure Estimate Model (DEEM™) in a probabilistic mode. The analysis evaluates individual food consumption as reported by respondents in the USDA 1989-1992 Continuing Survey of Food Intake by Individuals (CSFII) and accumulates exposure to the chemical for each commodity. This analysis is refined in that it uses monitoring data from USDA's Pesticide Data Program (PDP) and FDA Surveillance Monitoring Program to calculate anticipated residues for use in the acute dietary analysis. Data on the percentage of a crop-treated was obtained from the Biological and Economic Analysis Division (BEAD) for all commodities with diazinon tolerances included in the acute dietary assessment.

Risk estimates for acute dietary exposure based on existing uses do not exceed HED's level of concern. Risk estimates for all subgroups analyzed are below 100% of the acute population-adjusted dose (aPAD) at the 99.9th percentile of exposure. Currently, HED expresses acute risk as a percentage of the acute population-adjusted dose (% aPAD= (exposure ÷ aPAD) x 100). An exposure to this chemical relative to the acute dietary PAD of less than or equal to 100% of the aPAD does not exceed HED's level of concern. The acute dietary risk estimates (expressed as a % aPAD) are: for the general U.S. population, 37%; for all infants (less than 1 year old), 29%; and for children (1 to 6 years old), 63% (the most highly exposed subgroup).

The chronic dietary exposure analysis estimates the average exposure for the overall U.S. population and certain subgroups over a lifetime. The exposure analysis was performed using the Dietary Exposure Estimate Model (DEEM™) in a deterministic mode. The analysis evaluates individual food consumption as reported by respondents in the USDA 1989-1992 CSFII and accumulates exposure to the chemical for each commodity. Each analysis assumes uniform distribution of diazinon in the commodity supply. This analysis is refined in that it uses monitoring data from USDA's Pesticide Data Program (PDP) and FDA Surveillance Monitoring Program data to calculate anticipated residues for use in the chronic dietary analysis. Data on the percentage of a crop-treated was obtained from the Biological and Economic Analysis Division (BEAD) for all commodities with diazinon tolerances included in the dietary risk assessment.

Risk estimates for chronic dietary exposure from the registered uses of diazinon are well below 100% of the cPAD, and therefore, do not exceed HED's level of concern for any of the subpopulations analyzed. The chronic dietary risk estimates (expressed as a percentage of the chronic population-adjusted dose (cPAD) are: for the general U.S. population, 14%; for all infants (less than 1 year old), 12%; and for children (1 to 6 years old), 22%. This refined analysis used percent crop-treated data and anticipated residues based on USDA PDP and FDA monitoring data, and field trials.

Dietary Risk Estimates (Drinking Water)

Currently, HED uses drinking water levels of comparison (DWLOCs) as a surrogate measure of potential risks associated with exposure to pesticides in drinking water. A DWLOC is the concentration of a pesticide in drinking water that would be acceptable as a theoretical upper limit in light of total aggregate exposure to that pesticide from food, water, and residential uses (if any). A DWLOC may vary with drinking water consumption patterns and body weights for specific subgroups. In the absence of monitoring data on diazinon in drinking water, HED compares estimated peak and average concentrations of a pesticide in surface and ground water from conservative models to DWLOC values for acute and chronic assessments, respectively, in a screening-level assessment to semi-quantitatively estimate risk from exposure through drinking water. If screening-level model estimates are less than the calculated DWLOC values, there is no drinking water concern. This is considered a preliminary exposure assessment for the purposes of incorporating drinking water exposures into the human health risk assessment. This screening-level assessment has been refined by appropriate and applicable monitoring data when available. This approach is in accordance with "OPP's Interim Approach for Addressing Drinking Water Exposure", S. Johnson, 11/17/97.

Most monitoring efforts to date for diazinon in surface and groundwater have included the parent compound only. Previously, the HED Metabolism Assessment Review Committee (MARC) concluded that focusing on diazinon, *per se*, in water should be adequate for the purposes of risk assessment. This decision included consideration of the likelihood of occurrence in water of major soil and water metabolites that are toxicologically significant (HED MARC memorandum from D. Hrdy to G. Kramer dated 4/17/98). However, there is some indication that when drinking water is treated by chlorination, the toxic metabolite diazoxon is formed and that it may persist for up to 48 hours in finished water based on a recently published study (see 11/00 revised EFED chapter . Diazoxon residues were not included in the drinking water assessment at this time. To the extent that diazoxon, or other toxic degradates, may be present in finished drinking water, the resulting risk estimates would increase.

Acute Drinking Water Risk Estimates

Concentration estimates for acute exposures to diazinon in *groundwater* based on *model* estimates and *monitoring* data are less than the acute DWLOC values for all subgroups. HED concludes that there is no drinking water concern for acute exposures to diazinon in groundwater-sourced drinking water. Concentration estimates for acute exposures to diazinon in ambient *surface water* based on *monitoring* data are less than the acute DWLOC values for all subgroups. However, comparing acute DWLOC values to *model* estimates for concentrations of diazinon in surface water there is a potential concern for all population subgroups analyzed. Therefore, HED cannot conclude that there is no concern for exposures to diazinon in surface-water-sourced drinking water. Given the uncertainty in diazinon concentrations in surface water based on a comparison of the model estimates and monitoring data relative to each other (greater than 20x), and therefore, the uncertainty relative to diazinon concentrations in drinking water, HED recommends reassessing the potential acute exposure to diazinon in drinking water once sufficient surface water-sourced drinking water monitoring data on diazinon become available for use.

Chronic Drinking Water Risk Estimates

Concentration estimates for chronic exposures to diazinon in *groundwater* based on *model* estimates and *monitoring* data are less than the chronic DWLOC values for all subgroups analyzed. HED concludes that there is no drinking water concern for chronic exposures to diazinon in groundwater-sourced drinking water. Concentration estimates for chronic exposures to diazinon in ambient *surface water* based on monitoring data are less than the chronic DWLOC values for all subgroups. However, comparing chronic DWLOC values to *model* estimates for concentrations of diazinon in surface water there is a potential concern for all subgroups analyzed. Therefore, HED cannot conclude that there is no concern for exposures to diazinon in surface-water-sourced drinking water. Given the uncertainty in diazinon concentrations in surface water based on a comparison of the model estimates and monitoring estimates relative to each other (almost 20x), and therefore, the uncertainty relative to diazinon concentrations in drinking water, HED recommends reassessing the potential chronic exposure to diazinon in drinking water once sufficient surface-water sourced drinking water monitoring data on diazinon become available for use.

Occupational and Residential Exposure and Risk

Occupational and residential exposures to diazinon can occur during handling, mixing, loading and application activities. Occupational postapplication exposure can occur for agricultural workers re-entering treated fields such as during scouting, irrigation and harvesting activities.

Residential postapplication exposure can occur following treatment of lawns, or residences for cockroaches, and other insects. In addition, there is a potential for inadvertent oral exposure to children from placing fingers or objects in their mouths following contact with treated areas or incidentally ingesting diazinon-treated turf or soil. Postapplication exposure to children can occur in locations other than the home, including schools, daycare centers, playgrounds, and parks.

HED has conducted dermal and inhalation exposure assessments for: occupational and residential handlers; occupational postapplication; and residential postapplication exposure to adults and children. In addition, inadvertent oral exposure to children were evaluated. The exposure duration for short-term assessments is defined as 1 to 7 days. Intermediate-term durations are 1 week to six months, and long-term exposures are durations greater than six months. The duration of exposure is expected to be: short-, intermediate and in some cases long-term for agricultural handlers and occupational handlers in residential settings (i.e., lawn care operator and pest control operator); short and intermediate-term for occupational postapplication; and short-term for the residential handler. The postapplication residential exposures evaluated in this assessment are considered short-term, except for pet collar use, which is considered to be intermediate- and possibly long-term.

For the dermal and inhalation risk assessment, risk estimates are expressed in terms of the Margin of Exposure (MOE), which is the ratio of the NOAEL or LOAEL selected for the risk assessment to the exposure level. For short-term dermal risk estimates, margins of exposure or MOEs >100 (i.e., 10x for interspecies extrapolation and 10x for intraspecies variability) do not exceed HED's level of concern. For intermediate- and long-term dermal risk estimates, MOE > 300 (i.e., inter- (10X) and intra-species factors (10X), in addition to a 3X to extrapolate from a 21-day dermal study to longer-term exposures) do not exceed HED's level of concern. For inhalation risk assessments (all time periods) the target MOE is 300 resulting from the inter- (10x) and intra-species (10X) factors, and for lack of a NOAEL in the critical study and consequent use of a LOAEL (3x). The FQPA factor was reduced to 1X, therefore the same target MOEs are applicable to both occupationally exposed workers and adult and child residents.

Dermal and inhalation exposures were combined because of a common toxicity endpoint (i.e., cholinesterase inhibition), and because dermal and inhalation exposures may occur simultaneously. An aggregate risk index (ARI) was used to combine short-term dermal and inhalation risk estimates because the dermal and inhalation target MOEs are different (i.e., 100 for dermal and 300 for inhalation). An ARI of less than one exceeds HED's level of concern. However, a total MOE was calculated for intermediate- and long-term exposures because the target MOE is 300 for both dermal and inhalation exposure. For intermediate- and long-term aggregate exposure, an MOE of less than 300 exceeds HED's level of concern.

The **majority of occupational risk estimates for handlers** exposed to diazinon **exceed HED's level of concern**, even with PPE and/or engineering controls. HED identified 32 major handler scenarios, which when combined with a range of application rates resulted in 76 iterations within the 32 scenarios. The results of the agricultural handler assessments indicate that none of the potential exposure scenarios provide ARIs $1 for short-term durations or total dermal and inhalation MOEs greater than or equal to 100 and 300, respectively for intermediate and long-term durations at baseline attire (i.e., long pants, long sleeved shirts, no gloves). Only 5 of the short-term scenarios quantitatively evaluated using personal protective equipment (PPE) (long sleeved shirt, long pants, shoes, socks, chemical-resistant gloves, and dust/mist respirator) or by using engineering controls (e.g., closed mixing systems or enclose cabs) have a ARIs $1, while only 4 scenarios have total dermal and inhalation MOEs $300. There are insufficient data to adequately assess the sheep treatments, exterior paint additive uses and mushroom houses, and additional data are requested to support these uses. The agricultural handler assessments are believed to be reasonable representations of diazinon uses. Surrogate Pesticide Handlers Exposure Database (PHED) data were used to assess handler exposure because no chemical-specific studies are available, except for one study that evaluated application of dust formulation by a pest control operator (PCO) (MRID 44348801).

The results of the short- and intermediate-term **dermal postapplication assessments** for workers exposed to diazinon for most agricultural, and greenhouse activities indicate that MOEs are less than 100 at the current Worker Protection Standard (WPS)-required restricted entry interval (REIs) of 24 hours. Therefore, the majority of postapplication exposures exceed HED's level of concern. The MOEs for postapplication workers did not reach MOEs of 100 for 2-6 days after treatment for most vegetable crops, 3-8 days for fruit trees, 3-9 days for field crops, 3-7 days for berries, 6-8 days for ornamentals and 4-8 days for grapes. The REIs were based exclusively on dermal exposures because potential inhalation exposures were determined to be negligible in comparison. The potential for dermal contact during postapplication activities (e.g., harvesting) is assessed using a matrix of potential dermal contact rates by activity and associated crops. Chemical-specific dislodgeable foliar residue (DFR) data were submitted for cabbage and oranges. These data were used along with HED standard transfer coefficients derived from recently submitted Agricultural Reentry Task Force (ARTF) studies to assess potential exposures to workers reentering treated sites. The occupational postapplication assessment is believed to be reasonably representative of diazinon uses, except for nut trees and outdoor ornamental uses, which lack adequate transfer coefficient data.

Uncertainties in this analysis include: the use of a linear extrapolation applied to the DFR values from the study application rate (1 lb ai/A) to the maximum labeled rate (3 lbs ai/A) for tree crops; and the use of the available cabbage and citrus DFR values to estimate DFRs for other crops. The effect of extrapolating the cabbage and citrus DFR data to a higher application rate and using it to represent other crops is unknown and may under- or overestimate the actual residue levels.

All six short-term residential handler exposure scenarios evaluated have total ARIs using standard HED assumptions (i.e. short pants and 0.5 acre lawn size for liquid formulations) that **exceed HED's level of concern** defined by a target ARI of 1 (or MOE of 100 for biomonitoring results). The residential handler MOEs ranged from 3 to 520 for dermal risk, from 20 to 1,300 for inhalation risk, and total ARIs range from 0.03 to 2.4. The following scenarios were evaluated: (1,2) spot treatment of turf with liquid formulations using a low pressure handwand or backpack sprayer, (3,4) lawn treatment with liquid formulations using a ready-to-use (RTU) garden hose end sprayer or conventional hose end sprayer, and (5,6) lawn treatment with granular formulations via push-type spreader or belly grinder. For a number of scenarios, multiple evaluations were conducted using lawn size less than the 0.5 acre default (0.11 to 0.34 acres), application using different equipment or methods (i.e., ornamental treatment via low pressure hand wand and hose-end sprayer, and granular application via belly grinder and push-type spreader) or residents wearing long pants, to provide information for risk mitigation and management decisions. In some instances, when the product is only applied to 0.11 acres or residents wear long pants, the risk estimates do not exceed HED's level of concern.

A chemical-specific handler study was used to assess three scenarios (MRID 45184305). This study conducted both biomonitoring (i.e., urinary measurement of a unique diazinon metabolite, G27550) and/or passive dosimetry measurements on 42 different residential applicators. In addition, passive dosimetry exposure data from a recently submitted Occupational and Residential Exposure Task Force (ORETF) handler study with dacthal were used to assess conventional hose-end sprayer (dial type sprayer), RTU hose-end sprayer, and granular push-type spreader exposures (MRID 44972201). This study was used as a surrogate to assess diazinon. In the absence of chemical-specific data, HED relied on information from the Draft Residential Standard Operating Procedures (SOPs - December 1997), and updated assumptions (2000 SOPs). It was assumed that residential applicators wear short sleeve shirts, short pants, and no gloves.

For several residential handler scenarios, HED evaluated exposures and risks using both passive dosimetry and biomonitoring data from the same study. HED evaluated the biomonitoring data at both the central tendency (mean) and 90th percentile exposure estimates as measured in the study (i.e., treatment of 0.11 acres or 5,000 ft^2) because these exposures reflect actual measurements, and are not extrapolated or combined with default or high-end assumptions to estimate risks. In addition, HED extrapolated the passive dosimetry and biomonitoring data from 0.11 acres (as measured in the registrant study) to 0.5 acre in accordance with current Agency policy. In this instance, only the central tendency biomonitoring exposure estimates were presented (i.e., 90th percentile exposures are not extrapolated). As noted previously, all risk estimates for residential handlers that treat a 0.5 acre lawn size exceed HED's level of concern. The biomonitoring data represent total exposure, because they are based on a total absorbed dose resulting from primarily dermal and inhalation exposure. While biomonitoring data are typically preferred for assessing exposures, HED believes the biomonitoring results for diazinon may underestimate exposure and risk primarily due to possible incomplete urine collection for some individuals (at least 9 of 42 individuals appeared to have low urine volumes), in addition to lack of pharmacokinetic data for the G-27550 metabolite following dermal exposure. For these reasons, Canada's Pest Management Regulatory Agency (PMRA) does not consider the biomonitoring results to be acceptable for use in generating handler exposure estimates (personal communication with Kristen Macey, 11/21/00).

An important factor that contributes to the possible over-estimation of risk is that a 21 day inhalation toxicity endpoint based on whole body exposure in rats, and a 21 day dermal toxicity endpoint in rabbits were used to assess a short-term (hours to a single day) exposure scenarios.

The results of the **residential postapplication** exposure scenarios indicate that **all four** scenarios evaluated have short-term ARIs < 1 or intermediate-term total MOEs <300 for children, and therefore **exceed HED's level of concern**. These scenarios include exposures following indoor crack and crevice treatment, pet collar use, and liquid and granular lawn treatments. The ARIs that exceed HED's level of concern ranged from 0.03 to 0.04 for total dermal, inhalation and inadvertent oral (in the case of children) risk resulting from postapplication exposures on treated lawns. The majority of MOEs for indoor crack and crevice treatment for children and adults (inhalation MOEs=1.2-380, dermal MOEs= 0.04-2) and pet collar use (dermal MOEs=45-120 for children, 210-590 for adults) also exceed HED's level of concern. Several of the residential postapplication risks were estimated based on chemical-specific studies submitted by the registrant (i.e., crack and crevice treatment, and broadcast treatment of turf with diazinon liquid or granular formulated products) in conjunction with assumptions in the residential SOPs. As noted previously, in July 2000, the registrants agreed to discontinue to support the registration of indoor uses, including crack and crevice treatment, and pet collar use. Nevertheless, these scenarios are presented for a complete assessment. HED evaluated risks associated with both watered-in and non-watered in lawn treatment to assist risk management decisions, although the label only requires watering-in for granular products. The available data suggest that the risks associated with watered-in lawn treatment are lower than non-watered in treated lawns.

It is HED’s policy to routinely conduct screening level assessments (based on standard values in the Residential SOPs) for children’s incidental ingestion of granules when a granular pesticide may be applied in residential settings. The screening-level assessment for diazinon resulted in an MOE of 0.26 and is a risk estimate of concern. Information on particle density (number of particles per pound or gram), carrier type (corn cob, clay), granular color, and average granular size is requested from the registrant in order to refine this screening level assessment.

The ARI for children is conservative because it assumes a child is simultaneously conducting hand to mouth activities, ingesting soil and grass, dermally contacting the treated lawn and breathing diazinon residues in air the day of lawn treatment. Therefore, HED also evaluated aggregate dermal and inhalation exposures for children to evaluate the impact of excluding the oral pathways. The dermal and inhalation ARIs for the liquid formulation are mostly less than 1 (ARIs range from 0.2 to 1.24). However, the ARIs for granular turf treatment are mostly greater than 1 (ARIs range from 0.59 to 5), and therefore, do not exceed HED's level of concern, except for combined dermal and inhalation exposures for children in Pennsylvania (ARI=0.59).

There are uncertainties in the risk estimates that could over- or under-estimate the risks associated with postapplication lawn exposure. For example, the most important factors that contribute to the possible over- or under-estimation of risk are: (1) use of a 21 day inhalation toxicity endpoint based on whole body exposure in rats, or a 21 day dermal toxicity endpoint to assess a 2 hour lawn exposure scenario; (2) assumption that individuals contact treated turf for 2 hours the day of treatment (after the turf has dried for dermal and oral pathways), or inhale the volatilized residues immediately after treatment for inhalation (i.e., within 4 hours post application); (3) assumption that 5% of the application rate is available for transfer to hands from foliage (to account for wet or sticky hands) based on data from Clothier (1999), when turf transferable residue (TTR) data show only 0.049% is transferred onto dry cotton cloths (4) use of an inhalation rate of 0.7 m^3/hr for children 1-6 years of age, when there are few data available on this parameter for children less than 3 year (although protective for young children, this breathing rate could underestimate exposure and risks to children 6 years of age and older involved in moderate activities such as playing baseball, soccer, etc. for more than 1 hour the day of treatment); (5) the inhalation risk estimates are based only on aerosol concentrations and exlude vapor residues, which could be significant during diazinon volatilization; (6) this assessment does not assess potential exposures to all environmental metabolites; and (7) use of average air concentrations across three geographic locations to assess inhalation risk estimates following lawns treated with liquid formulations.

It should be noted that the diazinon air residues declined substantially (2-10 fold of initial air levels) within 8 hours of turf treatment for liquid formulation. In addition, the turf transferable residues dissipated rapidly over time, with residues non-detectable within 2 days postapplication. Therefore, the exposure and risk estimates on day 2 postapplication would be significantly less than the day of treatment exposure and risk estimates presented in this assessment.

In addition, the Residential SOPs are considered to be conservative scenarios for determining risk estimates. The adult and toddler transfer coefficients are based on the Jazzercise protocol and an upper percentile exposure duration value of 2 hours/day. The dermal exposure estimates, however, are more refined because they are based on actual TTR data compared to the incidental ingestion scenarios which are based on estimated grass and soil concentrations, in addition to estimated dislodgeable foliage residues (DFR) that assume 5% of the application rate could be transferred to a child's wet hands.

Aggregate Exposure/Risk

When target MOEs for multiple exposure pathways differ, but exposures across those pathways must be combined under an aggregate risk assessment, HED uses the Aggregate Risk Index method (ARI method). ARIs greater than 1.0 do not exceed HED's level of concern. Results of the specific aggregate risk assessments included in this document are provided below.

<u>Acute Aggregate Risk Estimates</u>

The aggregate risk assessment for acute exposures to diazinon includes one day exposures through food and drinking water, only. Exposures to diazinon from food sources (based on refined exposure estimates) and drinking water (based on surface and groundwater monitoring data and groundwater model estimates) do not exceed HED’s level of concern for acute dietary risk for any subgroup analyzed. However, if surface water *model* estimates are used in the assessment, risk estimates for all population subgroups exceed HED’s level of concern.

Given the uncertainty in the model and monitoring estimates relative to each other (greater than 20x) for surface water concentrations of diazinon, and therefore, the uncertainty relative to diazinon concentrations in actual drinking water, HED recommends that the acute exposures to diazinon in drinking water, and subsequently acute aggregate exposure, be reassessed once sufficient surface-water sourced drinking water monitoring data on diazinon and its toxic degradates become available for use.

Short-term Aggregate Risk

HED has concerns for aggregate short-term exposures to diazinon for residential handlers of lawn products. Risk estimates for handlers for combined dermal and inhalation exposures to diazinon from granular and liquid formulations used to treat lawns exceed HED's level of concern. HED also has concerns for short-term postapplication exposures to diazinon for adults and children in the home after indoor crack and crevice treatments and outside the home after liquid or granular lawn treatment.

Short-term aggregate risk assessments combine short-term residential exposures with average, dietary (food and drinking water) exposures. However, because all ARIs for exposures of residential handlers are below 1, and therefore exceed the Agency's level of concern, HED has not aggregated short-term exposures from food, drinking water and residential exposures. Aggregating additional exposures from food and drinking water with these residential exposures would only result in a risk estimate that would further exceed HED's level of concern. Until residential short-term dermal exposures can be mitigated for residential handlers, aggregate short-term risk estimates exceed HED's levels of concern.

Postapplication dermal and inhalation exposures to children from indoor (crack and crevice) and outdoor (lawn) treatments result in ARIs less than 1. Therefore, HED has not aggregated short-term exposures from food and drinking water with postapplication residential exposures. Aggregating additional exposures from food and drinking water with these residential exposures would only result in a risk estimate that would further exceed HED's level of concern. Until postapplication residential short-term exposures can be mitigated, aggregate short-term risk estimates for postapplication exposures to diazinon exceed HED's levels of concern.

Chronic Aggregate Risk

The chronic aggregate risk assessment for exposures to diazinon includes long-term, average exposures to diazinon through food and drinking. There are no residential uses that result in chronic exposure. Therefore, chronic aggregate risk estimates based on estimated exposures from food and groundwater are the same as those presented under the section on chronic drinking water risk estimates. HED concludes chronic aggregate exposures to diazinon in food and ground-water sourced drinking water do not exceed levels of concern.

Chronic aggregate risk estimates based on estimated exposures from food (based on refined exposure estimates) and surface water (based on ambient monitoring data) do not exceed HED's level of concern for chronic aggregate exposures to diazinon in food and surface-water sourced drinking water. However, *model* estimates for concentrations of diazinon in surface water indicate there is a potential concern for all population subgroups analyzed However, given the uncertainty in the model and monitoring estimates relative to each other (almost 20x) for surface water concentrations of diazinon, and therefore, the uncertainty relative to long-term concentrations of diazinon in actual drinking water, HED recommends that the chronic exposures to diazinon in drinking water, and subsequently chronic aggregate exposure, be reassessed once sufficient surface-water sourced drinking water monitoring data on diazinon and its toxic degradates become available for use.

Uncertainty:

In conclusion, HED notes that the following issues introduce uncertainty into the risk estimates. For acute and chronic dietary exposures, residue values in sheep fat, sheep meat, and beef fat are the major contributors to the risk estimates. Relative to other commidities in the dietary exposure, the residue values for these meat commodities are not highly refined. Better estimates of the percentage of sheep and cattle treated with diazinon (domestic and imported) will refine the exposure and risk estimates for both acute and chronic dietary assessments as would data reflecting residues in meat close to the point of consumption. Percent of crop-treated information for imported commodities may refine exposure and risk estimates. For drinking water exposures, additional monitoring data on diazinon and diazoxon in surface-water sourced drinking water, or more appropriately, finished drinking water, may clarify discrepancies between model estimates and monitoring data for diazinon in surface water and refine drinking water risk estimates. Estimates of long-term, average concentrations of diazinon in groundwater from monitoring data would allow refinement of chronic drinking water risk estimates. Pertinent information on toxicologically significant metabolites in drinking water would also reduce uncertainty in the risk estimates.

Data Requirements

The following data are required at this time:

Toxicology - The HIARC has determined that a 90-day repeated dose dermal toxicity study in rats be performed to support the conclusions from the 21-day dermal toxicity study in rabbits.

Product Chemistry - All pertinent generic data requirements are satisfied for the Novartis and Makhteshim "unstabilized" TGAIs, except that data pertaining to stability (OPPTS 830.6313) are outstanding for the Makhteshim TGAI and data concerning UV/visible absorption for the PAI (OPPTS 830.7050) are required for both TGAIs. All pertinent product-specific data requirements are satisfied for the Novartis 87% FI. Additional product-specific product chemistry data are required for the Prentiss 80%, 50%, 48.7%, 25%, and 10% FIs; the AgrEvo 10% and 5% FIs; and the Makhteshim 92% and 87% FIs. No product chemistry data have been submitted in support of reregistration of the Sureco 70.31%, 25%, and 12.5% FIs and the AgrEvo 25% FI. Data requirements for the repackaged Gowan and Drexel 87% FIs will be satisfied by data for the source products. The product chemistry data requirements for diazinon products are presented in the attached summary tables in the Residue Chemistry Chapter for diazinon. Refer to these tables for a listing of the outstanding product chemistry data requirements.

Residue Chemistry - Additional residue data are required for beans (lima), blueberries, celery, cucumbers, hops, dried peas, spinach, sugar beets, and Swiss chard. Additional residue data on sugar beets reflecting current label rates and PHI are necessary to determine if feed additive tolerances are necessary. Limited rotational crop studies on three representative crops are required.

Occupational Exposure - Handler and postapplication data requirements will be determined based on risk mitigation meetings with the registrant and growers. There are no chemical specific exposure data for diazinon sheep treatments, exterior paint additive uses and mushroom houses; therefore the Agency is requiring data and/or further clarification of the use patterns.

Mushroom houses: No data were submitted in support of postapplication exposures for workers re-entering mushroom houses. EPA has identified potential dermal and inhalation exposures resulting from this indoor application. The Diazinon 50W label (EPA Reg. No. 100-460) directions for mushroom houses is to use a spray dilution rate of 0.04 to 0.05 lb ai/gallon and apply "on outside and inside walls, floors and sideboards of mushroom houses after compost has been pasteurized by heating ... and spray over the plastic covering the beds and trays after spawning." Potential dermal exposures in mushroom houses may arise from workers contacting treated surfaces as all surfaces may be treated. The potential inhalation exposures may result from air concentrations of diazinon in the mushroom house resulting from the application before or after ventilation. Additional data are needed to estimate the potential for dermal exposure in mushroom houses including (1) identification of mushroom house activities that may result in dermal contact, (2) the residue levels on the sideboards and plastic covering the beds and trays, and (3) direct dermal exposure measurements or transfer coefficients. Additional data are also needed to determine air concentrations of diazinon over time. In lieu of air concentration data to calculate exposure/risk, HED determined an allowable air concentration based on the inhalation LOAEL of 0.1 mg/m3 from a 21-day whole body aerosol study exposing rats 6-hours per day and the uncertainty factor of 300. The estimated 6 hour time-weighted-average (TWA) allowable air concentration is 0.0003 mg/m3 (i.e., LOAEL of 0.1 mg/m3 divided by 300 UF). This calculation assumes that the rat and human activity level for a breathing weight is equivalent. The LOD from the air sampling portion of the diazinon lawn treatment study (MRID 449591-01) is listed as 0.0006 mg/m3 (see study results in this chapter for actual air concentration levels at specific time intervals).

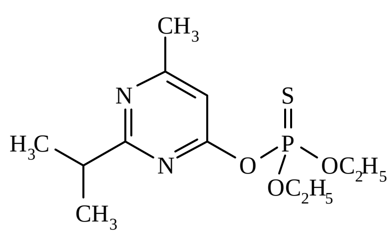
II. USE PROFILE

Diazinon [O,O-diethyl-O-(2-isopropyl-6-methyl-4-pyrimidinyl)phosphorothioate] is a nonsystemic organophosphate insecticide/acaracide registered for use on a variety of terrestrial foods and an aquatic food (watercress), livestock feeds, and livestock (sheep sprays and cattle ear tags). Since August 1986, label prohibitions against the use of diazinon on food crops grown in greenhouses have been required. It has registered non-food uses, as well, including: food/feed handling establishments, livestock areas, and indoor/outdoor residential sites. Diazinon has veterinary uses for fleas and ticks. Currently approved veterinary uses are for impregnating pet collars with diazinon. It is available in dust, granules, seed dressings, wettable powders, and emulsifiable solution formulations. It can be applied foliarly or as a soil treatment using ground or aerial equipment followed by incorporation for most uses. Based on available usage information, for 1987 through 1997, total annual domestic usage of diazinon is approximately 13 million pounds active ingredient. Most of this is allocated to outdoor residential uses, lawn care operators, and pest control operators. States with significant usage include California, Texas, and Florida.

III. PHYSICAL AND CHEMICAL PROPERTIES ASSESSMENT

A. <u>Description of Chemical</u>

Diazinon [O,O-diethyl-O-(2-isopropyl-6-methyl-4-pyrimidinyl)phosphorothioate] is a nonsystemic insecticide/nematicide.



Empirical Formula:	$C_{12}H_{21}N_2O_3PS$
Molecular Weight:	304.3
CAS Registry No.:	333-41-5
Chemical No.:	057801

B. <u>Identification Of Active Ingredient</u>

Pure diazinon is a colorless oil which is formulated into "stabilized" technical diazinon. Technical diazinon ($90% pure) is an amber to brown liquid with a boiling point of 83-84°C. Technical diazinon is practically insoluble in water (40 ppm at 20° C) but is completely miscible in acetone, benzene, dichloromethane, ethanol, 1-octanol, toluene, and xylene, and is soluble in petroleum oils.

C. <u>Manufacturing Use Products</u>

A search of the Reference Files System (REFS) conducted 9/15/99 identified 21 diazinon manufacturing-use products (MPs) registered under PC Code 057801. The registered diazinon MPs are listed in Table 1 and are the only products subject to a reregistration eligibility decision. We note that several products are manufactured from an unregistered "unstabilized" TGAI; data are required for the TGAI for the reregistration of diazinon.

Table 1. Registered Diazinon Manufacturing-Use Products.

Formulation	EPA Reg. No.	Registrant
87% FI	100-524	Novartis Crop Protection, Incorporated (formerly Ciba-Geigy Corp.)
56% FI	100-783	
22.4% FI	100-771	
5% FI	100-714	
80% FI	655-473	Prentiss, Incorporated
50% FI	655-463	
48.7% FI	655-500	
25% MAI FI [1]	655-595	
10% MAI FI [1]	655-401	
70.31% MAI FI [2,3]	769-695	Sureco, Incorporated
25% FI [4]	769-693	
12.5% MAI FI [2,5]	769-691	

Formulation	EPA Reg. No.	Registrant
25% MAI FI [1]	4816-685	AgrEvo Environmental Health (formerly Fairfield American Corp.)
10% MAI FI [1]	4816-640	
5% MAI FI [1]	4816-245	
5% MAI FI [1]	4816-621	
87% FI [6,7]	10163-212	Gowan Company
92% FI [6]	11678-6	Makhteshim Chemical Works Limited
87% FI [6]	11678-20	
87% FI [6,7]	19713-104	Drexel Chemical Company

1 Formulated with piperonyl butoxide and pyrethrins.

2 Formulated with aliphatic or aromatic solvents.

3 Transferred from Southern Mill Creek Products Company (EPA Reg. No. 6720-201; 12/18/92).

4 Transferred from Southern Mill Creek Products Company (EPA Reg. No. 6720-199; 12/18/92).

5 Transferred from Southern Mill Creek Products Company (EPA Reg. No. 6720-197; 12/18/92).

6 REFS currently identifies this product as a technical; however, it is correctly identified as an FI.

7 Repackaged from EPA-registered products.

D. Regulatory Background

Diazinon was the subject of a Reregistration Standard dated 7/15/86 which stated that generic and product-specific product chemistry data for all MPs must be resubmitted in support of the reregistration of diazinon. An Addendum #1 to the Product Chemistry Chapter was issued 8/22/86 which required preliminary analysis of all Ts and FIs for tetraethylpyrophosphate (TEPP) or sulfur derivatives of TEPP, upper certified limits for TEPP and sulfur derivatives of TEPP, and quantitative enforcement analytical methods with supporting validation data for products in which these impurities were identified. The Diazinon Reregistration Standard-Update #1 dated 3/24/88 reiterated the requirements specified in the Reregistration Standard and noted that because the "unstabilized" TGAI was stabilized for registration, the registered MPs would be classified as FIs. A Guidance Document was issued 12/88. Data submitted in response to the Update #1 and the Guidance Document were reviewed and summarized in the Diazinon Reregistration Standard Update dated 1/24/92. We note that the Novartis 56% and

22.4% FIs and the Gowan 87% FI were registered subsequent to issuance of the Update (3/18/96, 9/14/95, and 9/29/94, respectively).

The current status of the product chemistry data requirements for the diazinon products is presented in tables in the Product and Residue Chemistry Chapter (D270422, 12/00, D.Drew). Refer to these tables for a listing of the outstanding product chemistry data requirements.

E. Product Chemistry Requirements

All pertinent generic data requirements are satisfied for the Novartis and Makhteshim "unstabilized" TGAIs, except that data pertaining to stability (OPPTS 830.6313) are outstanding for the Makhteshim TGAI and data concerning UV/visible absorption for the PAI (OPPTS 830.7050) are required for both TGAIs. All pertinent product-specific data requirements are satisfied for the Novartis 87% FI. Additional product-specific product chemistry data are required for the Prentiss 80%, 50%, 48.7%, 25%, and 10% FIs; the AgrEvo 10% and 5% FIs; and the Makhteshim 92% and 87% FIs. No product chemistry data have been submitted in support of reregistration of the Sureco 70.31%, 25%, and 12.5% FIs and the AgrEvo 25% FI. Data requirements for the repackaged Gowan and Drexel 87% FIs will be satisfied by data for the source products.

Provided that the registrants submit the data required in the attached data summary tables for the unregistered "unstabilized" TGAIs and the registered MPs and either certify that the suppliers of beginning materials and the manufacturing processes for the diazinon TGAIs and MPs have not changed since the last comprehensive product chemistry review or submit complete updated product chemistry data packages, HED has no objections to the reregistration of diazinon with respect to product chemistry data requirements.

IV. HUMAN HEALTH RISK ASSESSMENT

A. Hazard Assessment

The toxicology data base for diazinon is sufficient to support the Reregistration Eligibility Decision (RED).

1. Acute Toxicity

Table 2 below summarizes the results endpoints, and toxicity categories for the acute toxicity studies.

Table 2. Summary of acute toxicity of technical Diazinon.

Guideline No.	Study Type	MRID No.:.	Results	Toxicity Category
81-1.	Acute Oral - Rats.	41407218	LD_{50} = M =1340 (1140-1610) mg/kg F = 1160 (999-1350) mg/kg Combined sexs = 1250 (1080-1415) mg/kg , 95% confidence limits)	III
81-2.	Acute Dermal - Rabbits.	41407219.	LD_{50} > 2020 mg/kg	III
81-3.	Acute Inhalation - Rats.	41407220.	LC_{50} = > 2.33 mg/L/4 hours	III
81-4.	Primary Eye Irritation - Rabbits.	41407221.	Minimally irritating.	III
81-5. :	Primary Dermal Irritation - Rabbits.	41407222.	maximum irritation score 2.8 (slight irritant)	III

Table 2. Summary of acute toxicity of technical Diazinon.				
Guideline No.	**Study Type**	**MRID No.:.**	**Results**	**Toxicity Category**
81-6.	Dermal Sensitization - Guinea pigs.	41407223 and 00232008	Not a sensitizer in guinea pig (Buehler assay). [Human study indicates 5-6/56 showed positive sensitization].	--
81-7. :	Delayed type neurotoxicity-hens.	44132701	No evidence of delayed type neurotoxicity	--

2. Subchronic Toxicity

i. 21- Day Dermal Toxicity in Rabbits (82-2).

In a 21-day dermal toxicity study in rabbits (MRID No.: 40660807), four groups of New Zealand strain rabbits (5/sex/dose) received repeated dermal applications of diazinon (97.1% suspended in 50% polyethylene glycol) at 0, 1, 5 and 100 mg/kg/day, 6 hours/day, 5 days/week over a 21-day period.. The high dose of 100 mg/kg/day was reduced to 50 mg/kg/day due to excessive toxicity which manifested as death in 4 of 5 males ; these animals exhibtied tremors and other signs of cholinergic reactions on days three to six prior to death.. The high dose was then reduced to 50 mg/kg/day. Hematology and clinical chemistry were assessed at termination. Serum cholinesterase and RBC and brain acetylcholinesterase was assessed by diagnostic kit (Berringer Mannheim Diagnostics). There were some indications of increased weight gain and food consumption in the rabbits dosed all doses of diazinon but there was no dose response and it considered that the data were too few animals on the study to make a more definite evaluation. The LOAEL for systemic toxicity is 100 mg/kg/day based on deaths related to cholinergic inhibition symptoms. The NOAEL is 50 mg/kg/day. Serum ChE in females demonstrated 32% ($p < 0.05$), 35% ($p< 0.01$) and 62% ($p < 0.01$) inhibition for the 1, 5 and 50 mg/kg/day dose groups respectively relative to the control group based on group means after three weeks. When compared to the predosing baseline, this progression was 16%, 18% and 57% ($p < 0.01$). Thus, there was no dose response between the 1 and 5 mg/kg/day dose groups. Statistical evaluation by HED staff using pair-wise analysis indicated that only the mid and high dose groups were statistically significant although a trend was evident for all groups. For males, statistically significant inhibition of plasma ChE was evident at 50 mg/kg/day only (64% $p < 0.05$) although there was 23% apparent inhibition at 5 mg/kg/day. RBC AChE was statistically significantly decreased at 50 mg/kg/day (39% for males and 32% for females, both $p < 0.01$). Brain AChE in females was decreased at 5 mg/kg/day (18% $p < 0.05$) and 50 mg/kg/day (43% $p < 0.05$. In males there was only one surviving rabbit and brain AChE was decreased 28%. The LOAEL for inhibition of serum ChE and brain AChE is 5 mg/kg/day based on data in females. The NOAEL is 1 mg/kg/day. The LOAEL for inhibition of RBC AChE is 50 mg/kg/day. The NOAEL is 5 mg/kg/day**.**

ii. Subchronic Oral Toxicity in Dogs (82-7): In a four-week pilot study (MRID 40815004), groups of 4/sex beagle dogs received diets containing diazinon (MG-8) at dose levels of 0, 0.5, 2, 20 or 500 ppm . These dose levels corresponded to 0.02/0.023, 0.073/0.082, 0.80/0.75 or 14.68/15.99 mg/kg/day for males/females. Plasma cholinesterase was inhibited at 0.5 ppm in females at approximately 29%, ($p < 0.01$) and in males at approximately 8% (not significant). Only at 500 ppm was red blood cell (26-39% in both males and females) and brain (44% in males, 50% in females) acetyl cholinesterase inhibited (all $p < 0.01$). Systemic toxicity was evident at 500 ppm only and included emesis and decreased body weight and feed consumption. For systemic toxicity, the NOAEL is 0.8 mg/kg/day and the LOAEL is 14.68 mg/kg/day based on decreases in body weight. For cholinesterase inhibition, the LOAEL is less than 0.023 mg/kg/day based on plasma cholinesterase inhibition; a NOAEL was not established..

In a 90-day study in dogs (MRID 40815004), groups of 4/sex beagles received diets containing diazinon (MG-8) at dose levels of 0, 0.1, 0.5, 150 or 300 ppm for 13 weeks. These doses correspond

to 0.0034/0.0037, 0.020/0.021, 5.9/5.6 or 10.9/11.6 mg/kg/day for males/females. Plasma cholinesterase was inhibited in females at 0.5 ppm at approximately 16% (not significant) and in males at approximately 30% ($p < 0.05$). At 150 ppm, plasma cholinesterase was inhibited about 80% in both males and females. At 150 ppm, red blood cell (~25% in males and ~31% in females, $p < 0.01$) and brain acetyl cholinesterase (31% in males and 30% in females) were inhibited. At 300 ppm, brain AChE was inhibited ~42% in males and ~45% in females.
For systemic toxicity, the NOAEL is 0.021 mg/kg/day and the LOAEL is 5.6 mg/kg/day based on deceased body weight. Systemic effects were noted at 150 ppm and included decreased body weight gain in females (34%, not significant), total protein (~1.4%) and calcium (~5%). At 300 ppm, both male and female body weight gain was decreased (33% males and 45% females), and decreased food consumption and total protein and calcium deceases were increased. For cholinesterase inhibition, the NOAEL is 0.0037 mg/kg/day and the LOAEL is 0.020 mg/kg/day based on plasma cholinesterase inhibition in males.

iii. Subchronic Inhalation in Rats (82-4): Groups of Sprague-Dawley rats (15/sex/concentration) were exposed to concentrations of diazinon (MG-8, 87% purity) at 0, 0.1, 1, 10 and 100 µg/L for 6 hours/day, 7 days/week for 21-days. No systemic toxicity was seen at any dose level. For systemic toxicity, the NOAEL is greater than 100 ug/L; a LOAEL was not established.. Exposure to diazinon resulted in the inhibition of cholinesterase activity at all concentrations.Exposure to diazinon resulted in plasma, red blood cell (RBC) and/or brainc cholinesterase inhibition (ChEI) at all concentration tested. There was a clear dose-depended decreases in ChEI for all three compartments in both sexes. At 0.1 : g/L: plasma ChEI was statistically significant ($p <0.05$) in males (30%) and females (56%); RBC ChEI was statistically significant ($p <0.05$) only in males (18%) but not in females (4%); and brain ChEI was not statistically significant in males (4%) or females (6%).At 1 : g/L: plasma ChEI was statistically significant ($p <0.05$) in males (50%) and females (71%); RBC ChEI was statistically significant ($p <0.05$) in males (53%) and females (45%); and brain ChEI was statistically significant ($p <0.05$) in males (13%) or females (15%). At 10 : g/L :plasma ChEI was statistically significant ($p <0.05$) in males

(60%) and females (76%); RBC ChEI was statistically significant ($p < 0.05$) in males (75%) and females (75%); and brain ChEI was statistically significant ($p < 0.05$) in males (37%) and females (44%). At 100 : g/L: plasma ChEI was statistically significant ($p < 0.05$) in males (80%) and females (88%); RBC ChEI was statistically significant ($p < 0.05$) in males (91%) and females (93%); and brain ChEI was statistically significant ($p < 0.05$) in males (62%) or females (80%). For plasam ChEI, a NOAEL is not established for males or females. For RBC ChEI, the NOAEL is 0.1 : g/L in females; a NOAEL is not established for males. For brain ChEI, the NOAEL is 0.1 : g/L for both sexes. For plasma ChEI, the LOAEL is 0.1 : g/L in both sexes. For RBC ChEI, the LOAEL is 0.1 : g/L in males and 1.0 : g/L in females. For brain ChEI, the LOAEL is 1.0 : g/L in both sexes.

3. Chronic Toxicity and Carcinogenicity

<u>i. Oral Toxicity Study in Rats - (83-1(a):</u> Sprague-Dawley strain rats (30/sex/dose) received diets containing diazinon (MG-8;87.7% purity) atdose levels of with 0.0 (two groups), 0.1, 1.5, 125 or 250 ppm diazinon) for 98 weeks (MRID 41942002). These dose levels correspond to 0.004/0.005, 0.06/0.07, 5/6 or 10/12 mg/kg/day for males/females. The control groups (both sets) and the 250 ppm dose group had satellite groups of 10/sex that were reserved for a 4 week recovery period following dosing for 52 weeks. No systemic toxicity was evident. Plasma cholinesterase was inhibited at 1.5 ppm in females (58%, $p < 0.01$) and in males (51%, $p < 0.05$ at termination only). It was noted that at 0.1 ppm at some assay intervals, females were inhibited <u>up to</u> 26% and males <u>up to</u> 36% but statistical significance was not attained. At 125 ppm, red blood cell cholinesterase was inhibited in males (28%, $p < 0.01$) and in females (26%, $p < 0.01$). Brain acetyl cholinesterase was inhibited at 125 ppm for males (24%, $p < 0.01$) and females (29%, $p < 0.01$). For systemic toxicity, the NOAEL is greater than 12 mg/kg/day; a LOAEL was not established. For cholinesterase inhibition, the NOAEL is 0.005 mg/kg/day and the LOAEL is 0.06 mg/kg/day based on of plasma cholinesterase inhibition.

<u>ii. Oral Toxicity Study in Dogs - (83-1(b):</u> Groups of beagle dogs (4/sex/dose) dogs were fed diets

containing diazinona (MG-8) at dose levels of 0, 0.1, 0.5, 150 or 300/225 ppm for 52 weeks (MRID 41942001). The high dose group was initiated at 300 ppm but was reduced after 14 weeks to 225 ppm. These dose levels corresponded to 0.0032/0.0037, 0.015/0.020, 4.7/4.5 or 7.7/9.1 mg/kg/day. At 0.5 ppm, plasma cholinesterase was inhibited in females 18-40% ($p < 0.01$). At 150 ppm, red blood cell cholinesterase was inhibited in males (25-34%, $p < 0.01$) and in females (26-33%, $p < 0.01$). Plasma cholinesterase was inhibited at 0.1 ppm (9-28%, $p < 0.05$) in females and at 0.5 ppm 5-25% ($p < 0.05$) in males. Brain acetyl cholinesterase was inhibited at 150 ppm in females (26%, $p < 0.05$) and males (15%, not significant). At 225/300 ppm, male brain inhibition reached 25% but was not significant while female brain inhibition reached 35% ($p < 0.05$). Systcemic toxicity was evident at 150 ppm based on decreased body weight gain (up to 64%) and food consumption (up to 27%) particularly in males and increased serum amylase (24-59%). For systemic toxicity the NOAEL is 0.02 mg/kg/day and the LOAEL is 4.5 mg/kg/day based on decreases in body weight gain. For cholinesterase inhibition, the NOAEL is 0.0037 mg/kg/day and the LOAEL is 0.02 mg/kg/day based on plasma cholinesterase inhibition in females.

<u>iii. Oral Toxicity in Rats - Two Years (83-2(a)</u>: In a carcinogenicity toxicity study (MRID 00073372),diazinon (98% purity) was administered to groups of Fischer 344 (50/sex) rats at either 400 or 800 ppm (estimated to be 20 and 40 mg/kg/day) for 103 weeks. The control group consisted of 25/sex untreated rats. No systemic effects were reported. The study itself did not provide a basis for concluding that adequate doses were assessed. The dose levels tested are well established from other studies to be moderately strong inhibitors of plasma ChE, RBC AChE and brain AChE. No evidence of compound related tumors was apparent in this study. For systemic toxicity, the NOAEL was 40 mg/kg/day; a LOAEL was not established. **There was no evidence of carcinogenicity** . The doses tested were judged to be adequate to assess the carcinogenic potential of diazion based on the known property of diazinon to be a moderate inhibitor of ChE/AChE in several other studies at the dose levels tested.

<u>iv. Oral Toxicity in Mice - Two Years (83-2(b)</u>: In a carcinogenicity toxicity study (MRID 00073372) diazinon (98% purity) was administered to 50/sex B63CF1 strain mice in their diets at dose levels of

100 or 200 ppm (estimated to be 14 and 29 mg/kg/day) for 103 weeks. The control group consisted of 25/sex untreated mice. No data on systemic effects were seen. **There was no evidence of carcinogenicity** . The doses tested were judged to be adequate to assess the carcinogenic potential of diazion.

4. Developmental Toxicity

i. Oral Teratology Study in Rats (83-3(a): In a prenatal developmental toxicity study (MRID No.: 00153017), four groups of 27 assumed pregnant rats (Charles River Crl. COBS™ CD™ (SD)(BR)) were dosed as control, 10, 20 or 100 mg/kg/day on days 6 through 15 of gestation. Diazinon (purity not specified) was suspended in 0.2% carboxymethyl cellulose and the rats were dosed by gavage at a rate of 10 mL/kg/day. The rats were sacrificed on day 20 of gestation. At 100 mg/kg/day maternal body weight gain was decreased particularly during the 6-10 day interval (-11±2 gms vs +14±2 gms for the control). After that interval the rats showed recovery but net gain was 25% less for the high dose group at sacrifice. For maternal toxicity, the NOAEL is 20 mg/kg/day and the LOAEL is 100 mg/kg/day based on decreases in body weight gain. The mean fetal weight in the 100 mg/kg/day dose group was increased (~6%) and the mean number of live fetuses in this groups was slightly reduced. There were also noted slight increases in pre and postimplantation loss. An increase in rudimentary T-14 ribs that was within historical control range was also noted. For developmental toxicity the NOAEL is 100 mg/kg/day (HDT); a LOAEL was not established.

ii. Oral Teratology Study in Rabbits (83-3(b): In a developmental toxicity study (MRID No.: 00079017) diazinon (89.2% purity suspended in 0.2% carboxymethyl cellulose) was administered by gavage (1 mL/kg) to four groups of assumed pregnant New Zealand White Rabbits at dose levels of 0 (vehicle control), 7, 25 or 100 mg/kg/day on days 6 to 18 of gestation. At 100 mg/kg/day there were 9 deaths in the group of 22 does (40.9%). Clinical symptoms including tremors and convulsions and body weight gain decreases as well as gastro-intestinal hemorrhages and erosions were noted. The LOAEL for maternal toxicity is 100 mg/kg/day based on deaths. For maternal toxicity, the NOAEL is 25 mg/kg/day and the LOAEL is 100 mg/kg/day based on mortality in dams. No compound related effects on the fetuses were evident. For developmental toxicity the NOAEL is greater than 100 mg/kg/day; a. LOAEL was not established.

5. Reproductive Toxicity

i. 2-Generation Reproductive Toxicity Study in Rats (83-4): In a multi generation reproduction study (MRID No.: 41158101), four groups of 30/sex Sprague-Dawley strain rats were dosed as control, 10, 100 or 500 ppm of diazinon (equivalent to 0, 0.67, 6.69 or 35.15 mg/kg/day in male, and 0, 0.77, 7.63 or 41.43 mg/kg/day in females) for 10 weeks and mated (1:1) to produce F1 litter pups. The F1 litters were culled and mated to produce the an F2 generation. In the parental groups, at 100 ppm there was deceased weight gain (5-6% persistent for males in the second parental group and transitory for females.). At 500 ppm there were tremors in females; decreased male and female mating and fertility indices (second parental group) and increased gestation length. Dystocia and death were slightly increased but not definitely associated with treatment. For parental/systemic toxicity, the NOAEL is 0.67 mg/kg/day and the LOAEL is 6.69 mg/kg/day based on decreased parental weight gain. . In the pups, at 100 ppm there was mortality and decreased weight gain during lactation. At 500 ppm there were decreases litter size and viable pups. For offspring toxicity, the NOAEL is 0.67 mg/kg/day and the LOAEL is 6.69 mg/kg/day based on pup mortality and decreased weight gain.

6. Mutagenicity (84-2).

The results of the mutagenicity studies are tabulated below:

Gene Mutation	
Salmonella typhimurium/ Escherichia coli. MRID No.: 41557404	Independently performed tests were negative in S.typhimurium strains TA1535, TA1537, TA98 and TA 100 and E.Coli strains WP2 $uvrA^-$ up to the highest dose tested (5000 µg/plate ± S9). The test was negative up to the cytotoxic levels (120 µ/ML -S9 and 60 µg/mL +S9)
Mouse lymphoma L5178Y $TK^{\pm}$ for- ward gene mutation assay. MRID Nos.: 40660802 and 41119701	This test was negative up to cytotocic levels (120 µ/ML -S9 and 60 µg/mL +S9)
Chromosome Aberration	
Mouse micronucleus assay. MRID No.: 40660805 and 41603201	Negative in male and female CD-1 mice up to lethal doses administered by gavage (60 or 120 mg/kg). No evidence of cytotoxic effect on the target cells.
Other Mutagenic Mechanisms	
In vitro sister chromatid ex- change (SCE) in human lymphocytes. MRID No.: 41577301	Study was weakly positive showing reproducible but not dose-related significant increases in SCE frequency over an S9-activated concentrations range of 6.68-66.8 µg/mL. Higher levels (200 µg/mL +S9 or 66.8 µg/mL -S9) were cytotoxic.
In vivo SCE male ICR mice MRID No.: 41687701	The test was negative at oral doses of 10-100 mg/kg. Overt toxicity and bone marrow cytotoxicity were apparent in the treated males at the highest dose tested.
In vivo SCE in female CD-1 strain mice. MRID No.: 43060601	The test was negative in female mice at oral doses of 150-175 mg/kg. Overt toxicity and bone marrow cytotoxicity were apparent in the treated females at concentrations $ 150 mg/kg.
Primary rat hepatocyte un- scheduled DNA synthesis. MRID No.: 41557405	Independently performed tests were negative up the highest dose tested (120 µg/mL). Higher levels ($ 163.1 µg/mL) were insoluble.

7. Metabolism (85-1)

In this study (MRID 41108901) a series of experiments were run with ^{14}C labeled diazinon in Sprague-Dawley strain rats. After 24 hours most of the ^{14}C was recovered in the urine (58.2% & and up to 93.3% %) and smaller amounts (<2.5%) in the feces. After 7 days recovery was 96.7% to 100.25% and < 1% of the label remained in the tissues. The highest level was in the blood. Three major metabolites were identified in the urine to indicate that diazinon is metabolized to liberate the pyrimidinyl group that is oxidized and excreted. Only trace amounts of parent diazinon were present in the urine or feces. Refer to DER for chemical identification of the metabolites.

8. Dermal Absorption (85-3)

In an vivo percutnesous study, adult human volunteers (6/ group) were dosed dermally with ^{14}C-Diazinon. The application site was washed with soap and water after 24 hours and tape stripped after 7 days. Total urine was collected for 7 days and analyzed for radiolabel. Five rhesus monkeys were dosed intravenusly with 14C-Diazinon and total urine and feces collected for 7 days. Urine and feces were analyzed for radiolabel. Rhesus urinary excretion of radiolabel (56%) was used to correct human urinary excretion of radiolabel as a measure of abosrbed dose. Dose distribution was as follows:

Group /Dose	Application Site	Formulation Vehicle	Skin Wash (%)	Tape Strip (%)	Urine (%)	Total Recovery (%)	Absorbed [a.] (%)
A/ 2ug/cm^2	Ventral forearm	Acetone	0.4566	0.0096	1.9983	2.4645	3.5584
B/ 2ug/cm^2	Abdomen	Acetone	1.4448	0.0060	1.8095	1.9603	3.2313
C/ 1.47ug/cm^2	Abdomen	Lanolin	0.3543	0.0421	1.2757	1.6721	2.2780

[a.] Corrected by iv rhesus urinary excretion

9. Neurotoxicity

i. Acute Neurotoxicity in Rats (81-8): In an acute neurotoxicity screening study (MRID No.: 43132201 and 43132204), groups of 15/sex rats (Sprague-Dawley) were dosed as control 2.5, 150, 300 or 600 mg/kg of diazinon (D-Z-N technical 88% purity) in corn oil by gavage. 10/sex/group were assigned to the main phase of the study to assess for clinical signs, FOB and motor activity; the other five were assessed for ChE/AChE activity. Plasma ChE was inhibited at all dose levels (27% for males and 47% for females in the .5 mg/kg dose group) and RBC AChE was inhibited at 150 mg/kg (83% for males and 76% for females) at the time of peak effect (about 9 hours postdosing). ChE was equivalent to the controls at day 15 but RBC AChE still remained inhibited for both males and females especially at the higher dose levels. Brain AChE was unaffected when assessed at day 15. The LOAEL for RBC AChE inhibition is 150 mg/kg. The NOAEL for RBC AChE inhibition is 2.5 mg/kg. The LOAEL for plasma ChE inhibition is < 2.5 mg/kg. Based on the FOB assessments, effects at 150 mg/kg included abnormal gait (3/10 males, 7/10 females), ataxic gait (3/10 females), decreased body temperature (-2.1%, females), decreased rearing counts (-33% females), stereotypy (3/10 females) and fecal consistency and stained fur (3/10 males). Numerous other FOB parameters were affected at 300 mg/kg and above, of these tremors (6/10 females and 5/10 males at 300 mg/kg) were noted and dehydration (6/10 females) were noted. Refer to DER for additional parameters affected. Motor activity was decreased for males (27%, not significant) and females (46% $p < 0.01$) at 150 mg/kg and above. Body weight gain in males was decreased in the 300 (25%) and 600 (29%) mg/kg dose groups. Deaths (2 males and 1 female) resulted at 600 mg/kg. No histopathological lesions attributed to treatment were indicated. The LOAEL for neurotoxicity is 150 mg/kg based mainly on ataxic gait and supported by other effects believed to be related to ChE/ACHE inhibition. The NOAEL for neurotoxicity is 2.5 mg/kg.

In a special study (MRID No.: 43132203) especially designed to establish a NOAEL for ChE/AChE, five groups of 15 Sprague-Dawley rats/sex were dosed as control, 2.5, 150, 300 or 600 mg/kg diazinon MG87% (D*Z*N, 88% purity) by gavage in corn oil and were sacrificed in groups of 5/sex after 3, 9 or 24 hours. These intervals were designated as pre-peak, peak and post-peak for effects. The rats were assessed for clinical signs and for plasma ChE, RBC and brain AChE. Clinical signs were first evident in the 300 mg/kg dose group males at 9 hours and at 600 mg/kg at 3 hours. Males were more frequently affected than females. Plasma ChE was inhibited at 2.5 mg/kg by 30% for males and 60% for females after 9 hours and to a lesser extent at the other intervals. 66-91% inhibition was noted for all other intervals at higher doses. RBC AChE was inhibited 40% ($p < 0.01$) in females dosed with 2.5 mg/kg and 42 to 82% at the higher doses for all other intervals. Four brain regions (cerebellum, cerebral cortex, striatum and hippocampus) and the spinal cord were also assessed. Definite brain AChE inhibition (31 to 68%) was noted at 150 mg/kg in all four regions and the spinal cord. Thus, the LEL for plasma ChE and RBC AChE is < 2.5 mg/kg for both sexes but the NOEL and LEL for brain AChE are 2.5 and 150 mg/kg. Limited correlation between enzyme inhibition with symptoms was apparent since at 9 hours the symptoms were maximal and inhibition (> 77% in brain, >74% in RBC and >77% in plasma at 600 mg/kg) were reported but the enzymes remained inhibited when the symptoms regressed at 24 hours.

In another study (MRID No.: 44219301) conducted in two parts, to assess for the cholinesterase NOAEL and LOAEL and neurotoxicity reponeses following acute administration. In Part 1, behavioral effects and potential for inhibition of ChE/AChE of Diazinon MG87% was assessed in Sprague-Dawley Crl:CD BR/VAF/Plus strain rats. <u>Part 1 (behavioral effects)</u>, four groups of 5 rats/sex were dosed with 0, 100, 250 or 500 mg/kg of diazinon (undiluted) and additional groups of females were dosed with 25 or 50 mg/kg and the rats observed for clinical signs for 14 days. At 100 mg/kg, females were noted to have one incident of hypoactivity. At 250 and/or 500 mg/kg, miosis, hypoactivity, fur staining, and/or loss of pain reflex and at 500 mg/kg there was one death. These findings were corroborated by the ChE/AChE part of the study which also demonstrated miosis at 100 mg/kg in a single male rat. The LOAEL is 250 mg/kg based on miosis and hypoactivity. The NOAEL is 100 mg/kg but this is considered a threshold dose level.

In <u>Part 2 (ChE/AChE effects)</u>, Seven groups of males were dosed as control, 0.05, 0.5, 1, 10, 100 or 500 mg/kg and seven groups of females were dosed as control, 0.05, 0.12, 0.25, 2.5, 25 or 250 mg/kg and sacrificed ~24 hours later. Observations on their behavior reactions were noted and the blood and brain were assessed for ChE/AChE. The precision of the ChE/AChE assays was considered fair to poor but not sufficiently poor to preclude an assessment of the potential for diazinon to inhibit ChE/AChE. Plasma ChE was inhibited at 2.5 mg/kg in females (61%) and at 10 mg/kg in males (44%). RBC AChE was inhibited at 25 mg/kg in females (35%) and at 100 mg/kg in males (49%). Brain AChE was inhibited at 25 mg/kg in females (36%, not significant) and at 250 mg/kg (70%) and at 500 mg/kg in males (69%). The LOAEL is 2.5 mg/kg based on 61% plasma ChE inhibition in females. The NOAEL is 0.25 mg/kg.

<u>ii. Subchroni Neurotoxicity in Rats (82-8):</u> In a subchronic neurotoxicity study (MRID No.: 43549302) 5 groups of 15/sex Sprague-Dawley Crl CD[R] BR strain rats were dosed as controls, 0.3, 30, 300 or 3000 ppm corresponding to approximately 0.018, 1.8, 18 and 180 mg/kg/day of D*Z*N diazinon MG87% for 90 days with periodic assessments for clinical signs and FOB, motor activity and blood ChE/AChE. Regional brain AChE activity and neurohistopathology were assessed at termination. Principal clinical signs included (muscle fasciculations, 8/15 females; hyper-responsiveness and tremors, decrease in grip strength: 15-20% in males and 14-39% in females); body weight and gain and food consumption decrease in both sexes were noted at 3000 ppm only. The LOAEL for systemic and neurotoxicity effects is 3000 ppm (180 mg/kg/day) based on weight gain decrease and signs of nervous system perturbation. NOAEL is 300 ppm (18 mg/kg/day). At 30 ppm, plasma ChE (79%-86% in females, 37%-45% in males) and RBC AChE (53-60% in females and 37%-75% in males) and brain AChE cerebral cortex/hippocampus only (25% in females) were inhibited. Other regional brain AChE sources were inhibited at 300 ppm (55%-75% in females) but only at 3000 ppm in males 62% - 73%). Conclusions regarding inhibition of brain AChE are deferred to an accompanying study (MRID No. 43543901) which was especially designed to assess regional brain AChE inhibition. The LOAEL for plasma ChE and RBC AChE inhibition is 30 ppm and the NOAEL is 0.3 ppm.

10. Human Data

In a special study with humans (males only), groups of 3 volunteers were dosed with 0.02 or 0.025 mg/kg/day of diazinon (a.i. from Diazinon 50WP) in corn starch by capsule for 38 or 43 days (MRID 00091536). A control group of 3 was dosed with corn starch only. The LOAEL was 0.025 mg/kg/day based on plasma cholinesterase inhibition. The NOAEL was 0.02 mg/kg/day. Frequent assessments were made every 2 to 3 days of the blood for plasma cholinesterase and red blood cell acetyl cholinesterase. All three volunteers showed inhibition ranging from 8 to 38% in the 0.025 mg/kg/day dose group. Although two of the three volunteers dosed with 0.02 mg/kg/day showed consistent depression ranging from 9 to 30% of plasma cholinesterase relative to their pretest values, a definite conclusion of significant plasma cholinesterase inhibition could not be established. Red blood cell acetyl cholinesterase was not inhibited.

On January 14, 1999, the HIARC evaluated the study conducted in humans subjects with diazinon (MRID 00091536) and classified this study as *unacceptable* because an audit carried out in1980 (Clements report) classified this study as "INVALID" based on the following findings: 1) no physician oversight; 2) no rationale for the 'normalization' factor used in data reporting; 3) no analysis of capsules or record of specific dose administered; and 4) no raw data available.

B Dose Response Assessment

1. Special Sensitivity to Infants and Children

Prenatal developmental toxicity studies in rats and rabbits provided no indication of increased susceptibility of rats or rabbit fetuses to *in utero* exposure to diazinon. There was no indication of increased susceptibility in the fetuses as compared to parental animals in the two generation reproduction study. In the prenatal developmental studies, no developmental toxicity was seen at the highest dose tested, and in the two-generation reproduction study, effects in the offspring were observed only at treatment levels which resulted in evidence of parental toxicity. On the basis of the weight-of-the-evidence, it was determined that a developmental neurotoxicity study is not required (RfD Report date 6/17/97).

The FQPA Safety Factor Committee met on June 15 and 16, 1998 to evaluate the hazard and exposure data for diazinon and recommend application of the FQPA Safety Factor (as required by Food Quality Protection Act of August 3, 1996), to ensure the protection of infants and children from exposure to these pesticides.

The FQPA Safety Factor Committee has determined that the 10x FQPA safety factor can be reduced to 1x for diazinon based on the following factors (FQPA Safety Committee Report dated August 6, 1998):

(a) In prenatal developmental toxicity studies following *in utero* exposure in rats and rabbits, there was no evidence of developmental effects being produced in fetuses at lower doses as compared to maternal animals nor was there evidence of an increase in severity of effects at or below maternally toxic doses.

(b) In the pre- and postnatal two-generation reproduction study in rats, there was no evidence of enhanced susceptibility in offspring when compared to adults (i.e., effects noted in offspring occurred at maternally toxic doses or higher).

(c) There was no evidence of abnormalities in the development of the fetal nervous system in the pre/post natal studies.

(d) There is no concern for positive neurological effects from the available neurotoxicity studies or for histopathology in the central nervous system from the other toxicological studies (e.g., subchronic rat, chronic dog, chronic mouse and rat).

(e) The toxicology data base is complete and there are no data gaps according to the Subdivision F Guideline requirements.

(f) Adequate actual data, surrogate data, and/or modeling outputs are available to satisfactorily assess dietary and residential exposure and to provide a screening-level drinking water exposure assessment.

2. Toxicology Endpoint Selection

On July 27, 1998, the Agency announced that it is deeply concerned about the conduct of pesticide health effects on human subjects and consulted with the FIFRA Scientific Advisory Panel and the Scientific

Advisory Board (SAP/SAB) about the application of stringent ethical standards to any studies. The SAP/SAB discussed the use of the human studies at their meeting on December 10 and 11, 1998. At this time, the Agency has not yet received the response to its consultation with the SAP/SAB and is continuing to work on its approach to the critical ethical questions. It is current Agency policy to make no final regulatory decision based on a human study until a new policy has been developed to ensure that such studies meet the highest scientific and ethical standards.

In light of the developing Agency policy on use of toxicology studies employing human subjects, and pending reassessment of human studies for considerations of the ethical acceptability of such studies, HED has reconsidered the toxicology database for diazinon and has for the chronic dietary, as well as, occupational and residential dermal exposure risk assessments, used toxicology endpoints from animal studies**.**

On February 16, 1999 and again on March 4, 1999, the Health Effect Division's (HED) Hazard Identification Assessment Review Committee (HIARC) reviewed the toxicology database for diazinon and selected doses and toxicology endpoints for risk assessment, based solely on animal toxicity studies as presented in Table 3.

On October 5, 2000, the HIARC reevaluated the doses and toxicity endpoints selected for dermal exposure risk assessments at the previous (February/March, 1999) meeting based on the comments received during Phase 3 (Public Comment) of the Tolerance Reassessment Advisory Committee (TRAC) process. The Registrant contends that the Agency should not use the default assumption of 100% dermal absorption factor for diazinon to modify the oral dose when performing dermal risk assessments. The HIARC previously selected the 100% dermal absorption value based on the similarity of results seen following oral and dermal administration. The Registrant stated that data from the human study support the use of a 3.58% dermal absorption factor. In addition, the Registrant also submitted data from an exposure monitoring of homeowners mixing and applying readily available liquid products to their lawn. In one phase of the study (passive dosimetry), external exposure (dermal and inhalation) to diazinon was determined In the second phase of the study (urine biomonitoring), internal exposure to diazinon was based on their urinary excretion of G-27550, the major and unique metabolite of diazinon. The percent dermal absorption of diazinon determined by comparing the internal absorbed diazinon dose to the external diazinon dermal exposure. The registrant stated that data from this study showed that the dermal absorption of diazinon is 6.1%. Thus, the Registrant stated that a weight-of-evidence support a dermal absorption factor of 3.58 % based on an *in vivo* percutaneous absorption study of dizinon in human volunteers and new data from an exposure monitoring study of homeowners applying diazinon products. The Registrant contends that data from this study showed that the dermal absorption of diazinon is 6.1%. However HED conducted an independent analysis of this study and concluded that dermal absorption was highly variable (range <1 to 58%) depending on the individual techniques and application equipment used. This conclusion was based on comparing the passive dosimetry and biomonitoring exposures for the same individual. Average dermal absorption ranged from 4 to 14% (See Memorandum from D. Smegal to D. Drew/B. Chamblis, dated November 29, 2000, D268247). The HIARC reviwed these data at the October 5, 2000 meeting and revised the toxicity endpoints selected for dermal risk assessments; the HIARC also selected endpoints for incidental oral ingestion exposure scenarios. The endpoints selected at this meeting are presented in Table 3.

a. Acute Dietary (Acute Reference Dose)

An acute reference dose (0.0025 mg/kg/day) was derived from an acute neurotoxicity study in the rat. Doses based on the endpoint of cholinesterase inhibition were selected from this study for use in the acute dietary risk assessment. The LOAEL is 2.5 mg/kg/day based on 61% plasma cholinesterase inhibition in females. The NOAEL is 0.25 mg/kg/day. The uncertainty factors selected for this risk assessment were 10x for intra-species uncertainty and 10x for inter-species uncertainty for a total uncertainty factor (UF) of 100x. The additional safety factor for special sensitivity in infants and children was reduced to 1x. The resultant acute population-adjusted dose for acute dietary risk assessment is:

Acute PAD = 0.25 mg/kg/day (NOAEL) ÷ 100 (UF) = **0.0025 mg/kg/day**

As per current Office of Pesticide Programs (OPP) policy, the acute reference dose (RfD) modified by an FQPA safety factor is referred to as the Acute Population-Adjusted Dose (aPAD). Because the FQPA safety factor was reduced to 1x for diazinon, the acute PAD is equal to the acute RfD.

b . Chronic Dietary (Chronic Reference Dose)

A chronic reference dose was derived from the results *in toto* from seven oral feeding studies (in dogs from 4 week, 90-day, and 1-year feeding studies, and in rats from a 28-day feeding study, a 90-day feeding study, a 90-day neurotoxicity study, and a 2 year feeding study). Results from these studies demonstrated that the 0.02 mg/kg/day dose level was consistent with a pattern of no adverse effects. The uncertainty factors selected for this risk assessment were 10x for intra-species uncertainty and 10x for inter-species uncertainty for a total uncertainty factor (UF) of 100x. The additional safety factor for special sensitivity in infants and children was reduced to 1x. The resultant chronic population-adjusted dose for chronic dietary risk assessment is:

Chronic PAD = 0.02 mg/kg/day (NOAEL) ÷ 100 (UF) = **0.0002 mg/kg/day**

As per current Office of Pesticide Programs (OPP) policy, the chronic reference dose (RfD) modified by an FQPA safety factor is referred to as the Chronic Population-Adjusted Dose (cPAD). Because the FQPA safety factor was reduced to 1x for diazinon, the chronic PAD is equal to the chronic RfD.

In the first three studies in rats, the 0.02 mg/kg was clearly established as a NOAEL based upon statistically significant plasma cholinesterase inhibition at the next higher doses. In the two year feeding study, the dose levels did not include a 0.02mg/kg level, but the lowest two doses, 0.004/0.005 mg/kg in males and females, respectively and 0.06/0.07 in males and females, respectively, bracketed this level. Although at the 0.06 mg/kg level there was statistically significant depression in plasma cholinesterase in females in 4/5 time point measurements, the males (0.07 mg/kg) showed much more variability at this dose and had statistically significant plasma cholinesterase depression only in 1/5 time point measurements. At the lowest dose, 0.004 mg/kg, the males exhibited the same variability in plasma cholinesterase measurement although none of the levels reached statistical significance. Given the fact that there is no consistent pattern of plasma cholinesterase between the sexes, and the 0.06 mg/kg level appears to be a minimal effect level while the 0.004 mg/kg level is clearly a no-effect level, the 0.02 mg/kg level, common to the other three studies, was judged to be an overall NOAEL level for the rat.

The data for the dog which were considered included: a 4-week pilot feeding study, a 90-day feeding study and a one-year feeding study. Each of these studies had a common dose level of 0.02 mg/kg. In each of these studies the only effect seen at that dose level was plasma cholinesterase inhibition. In the 4-week pilot only females had a statistically significant inhibition of plasma cholinesterase which appeared to reach steady state between 14-25 days of dosing. In the 90-day study only males had a statistically significant inhibition of plasma cholinesterase at 0.02 mg/kg and only on days 29 and 86. In this study, steady state levels of plasma cholinesterase inhibition were reached between days 30 and 90. In the one year study, there were statistically significant decreases in plasma cholinesterase in females in 2/4 time point measurements at the lowest dose of 0.0037, but these decreases were considered not biologically relevant because of the inconsistency across time, and the variability of the magnitude of the decreases. At the next dose, 0.02 mg/kg, the only effect observed was statistically significant plasma cholinesterase inhibition in females across all time points and in males only midway in the study at day 176. No other effects were seen in any of the studies at the 0.02 mg/kg dose. The plasma cholinesterase inhibition at 0.02mg/kg is considered to be a minimal or borderline effect in the dog since there were no effects on either the blood or brain cholinesterase levels, and there was no consistent pattern of cholinesterase inhibition between the sexes at this level.

In summary, using a weight-of-the-evidence approach, the chronic dietary endpoint is based upon the results of seven studies in the dog and rat which point to 0.02 mg/kg/day as the appropriate level on which to conduct the chronic dietary risk assessment. Although 0.02 mg/kg/day was selected based on the results of short- and long-term studies, no additional uncertainty factors were deemed necessary since: 1) the principal effect (plasma cholinesterase inhibition) was considered to be minimal or borderline, primarily there were no other effects observed at this dose (e.g., no red blood cell or brain cholinesterase inhibition nor clinical signs of toxicity or systemic effects), and there was no consistent pattern of cholinesterase inhibition between the sexes at this level; 2) a steady state of plasma cholinesterase inhibition was reached by 30 to 90 days in the dog; and 3) this dose (0.02 mg/kg/day) was a clear NOAEL in rats.

c. Carcinogenicity Classification

In accordance with the Agency's 1996 Proposed Cancer Risk Assessment Guideline, diazinon is classified as a **"not likely human carcinogen"** based on the lack of evidence of carcinogenicity in mice and rats

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d. Dermal Absorption Factor

In the percutaneous dermal absorption study in humans, dermal absorption ranged from 2 to 4%, with a mean of 3.5%. This study, however, failed to account for 97% of the radioactive dose.

The biomonitoring/passive dosimetry study (MRID 45184305) showed that the estimated dermal absorption ranged from less than 1% to 58%, with mean of 4%-14%, depending on individual techniques and application equipment used. This conclusion was based on comparing the passive dosimetry and biomonitoring exposures for the same individual. Average dermal absorption ranged from 4 to 14% (See Memorandum from D. Smegal to D. Drew/B. Chamblis, dated November 29, 2000, D268247).

The comparison of the LOAELs based on a common toxicity endpoint (death) in the oral developmental toxicity study in rabbits and the dermal toxicity study in rabbits indicated 100% dermal absorption.

Thus, there was no consistency across species with regard to dermal absorption and the differences in the dermal absorption across species may be due to the pharmacokinetics and metabolism in each species as well as the susceptibility of the rabbit to diazinon once it is absorbed.

A dermal absorption factor is not required/applicable since a NOEAL established in a repeated dose dermal toxicity study was selected for dermal exposure risk assessments.

e. Dermal Exposure Risk Assessment (Short, Intermediate and Long Term).

The dose selected for short, intermediate and long-term dermal exposure risk assessements is the NOAEL 1 mg/kg/day based on inhibition of serum (-35%) and brain (-18%) cholinesterase activity in females at 5 mg/kg/day (LOAEL) established in the 21-day dermal toxicity study in rabbits.

For short-term (1-7 days) exposure risk assessments, the Level of Concern in a Margin of Exposure (MOE) of 100.

The HIARC determined that this study can also be used for intermediate and long-term exposure risk assessments since cholinesterase inhibition was seen following repeated dermal exposure. The HIARC, however, recommended that an additional 3x uncertainty factor (i.e., a Margin of Exposure of 300) be required for these scenarios. A MOE of 300 is required since the duration of treatment in the 21-day study may not be adequate to address the concern for achieving a steady-state following longer exposure. It was noted that in the 90 day oral studies in dogs, examination of the pattern of plasma ChE activity over time indicated that a steady state level of inhibition was reached by 90 days. This observation was supported by a similar examination of the blood cholinesterase data in the 1 year study in dogs which also contained a measurement time point at approximately 90 days.

In general, dermal toxicity studies of thio-organophosphate conducted in rabbits tend to under estimate the toxicity of the chemicals because rabbits possess high concentrations of plasma esterases which deactivage the chemical before it is converted into the active oxon. Diazinon is a thio-organophosphate which requires activation to the oxon in order to inhibit cholinesterase, and therefore, the 21-day dermal toxicity study in rabbits was not previously used for dermal risk assessments.

However, a closer re-examination of the results of the 21-day dermal toxicity study indicate that diazinon may be an exception to this hypothesis because: 1) adequate dermal absorption was demonstrated which in turn resulted in dermal toxicity; 2) the principal toxicological effect (serum and brain cholinesterase inhibition) was seen following repeated dermal exposure; 3) comparable toxicity (mortality) was noted following oral (developmental toxicity) and dermal exposures at the same dose (100 mg/kg/day); and the endpoint of concern is obtained from a route-specific study. For these reasons, the HIARC determined that in the case of diazinon it is appropriate to use this study for dermal risk assessments. HIARC is aware that in the rat plasma cholinesterase inhibition occurrs at a lower level following oral dosing. Therfore, the HIARC determined that a 90-day repeated dose dermal toxicity study in rats should be performed to verify and refine this conclusion. The rat was selected since this species is considered tohave dermal absorption properties closer to the human than rabbit and a 90-day interval was chosen to allow for sufficient time for maximum inhibition of plasma, red blood cell and/or brain cholinesterase activityity.

f. Inhalation (Short, Intermediate and Long-Term)

The dose selected for use in risk assessments based on inhalation exposures for any time period of exposure is 0.026 mg/kg/day based on the inhibition of plasma cholinesterase in both sexes and red blood cell cholinesterase inhibition in males. This endpoint is based on a LOAEL of 0.1 ug/L that was derived from the 21-day inhalation toxicity study in rats. One hundred percent absorption (100%) is assumed for the risk assessments. The equation below shows the conversion from the endpoint (dose) in ug/L to mg/kg body weight/day.

$$\frac{\text{0.1 :g/L x 10.26 L/hr (RV) x 6 hrs/day (duration) x 1 :g/1000 mg (conversion)}}{\text{0.236 kg (body weight)}} = \text{0.026 mg/kg/day.}$$

This dose should be used for risk assessments based on short-, intermediate-, and long-term inhalation exposures. TheLevel of Concern is a MOE of 300 which includes the conventional 100 and an aditional 3x factor for the use of a LOAEL (i.e., lack of NOAEL in the critical study). Therfore, a MOE greater than 300 would not exceed HED's level of concern.

Table 3. Summary of Toxicity Endpoint Selcted for Risk Assessments			
EXPOSURE SCENARIO	**DOSE (mg/kg/day)**	**ENDPOINT**	**STUDY**
Acute Dietary	NOAEL= 0.25	Plasma cholinesterase inhibition	Acute Neurotoxicity - Rat Special Study-Rat
	UF =100x FQPA = 1x	**Acute PAD = 0.0025 mg/kg/day**	
Chronic Dietary	NOAEL= 0.02	Consistent pattern of no adverse effects on cholinesterase inhibition.	4 week, 90 day and 1-year studies in dog 4 week, 90 day and 2 -year studies in rat
	UF= 100x FQPA = 1x	**Chronic PAD = 0.0002 mg/kg/day**	
Incidental Oral Ingestion- Short-Term	NOAEL = 0.25	Plasma cholinesterase inhibition	Acute Neurotoxicity - Rat Special Study-Rat
Incidental Oral Ingestion- Long-Term	NOAEL= 0.02	Plasma cholinesterase inhibition	90 day and 1-year toxicity-Dog
Dermal Short [a]**,** Intermediate and LongTerm [b]	NOAEL = 1	Plasma and brain cholinesterase inhibition.	21-day dermal toxicity-Rabbit
Inhalation Short, Intermediate and Long-Term [c]	LOAEL=0.1 : g/L = 0.026 mg/kg/day MOE of 300 required	Plasma and RBC cholinesterase inhibition	21-Day Inhalation - Rat

[a] = The Level of Concern is a MOE of 100 for short-term dermal exposure risk assessments

[b] = The Level of Concern is a MOE of 300 for intermediate and long-term dermal exposure risk assessments

[c] = The Level of Concern is a MOE of 300 for short, intermediate and long-term inhalation exposure risk assessments

3. Dietary Exposure and Risk Characterization

a. Dietary Exposure - Food Sources

A search on the Agency's Reference Files System (REFS) on 09/15/99 indicates that there are twelve diazinon end-use products registered to Novartis with food/feed uses. These products are presented below.

EPA Reg No.	Label Acceptance Date	Formulation Class	Product Name
100-445	6/90	2% D	D.Z.N. Diazinon 2D
100-456 [a]	8/96	2 lb/gal EC	D.Z.N. Lawn and Garden Insect Control
100-460 [b]	2/97	50% WP	D.Z.N. Diazinon 50W Insecticide
100-461	3/97	4 lb/gal EC	D.Z.N. Diazinon AG500
100-463	4/96	4 lb/gal EC	D.Z.N. Diazinon 4E
100-469	7/96	14% G	D.Z.N. Diazinon 14 G
100-528 [a]	10/96	5% G	D.Z.N. 6000 Lawn and Garden Insect Control
100-926	9/98	2% D	D.Z.N. Diazinon Garden Insect Dust
100-687	11/96	0.4 lb/gal EC	D.Z.N. 5.0 EC
100-770 [a]	10/96	2 lb/gal EC	D.Z.N. Diazinon Lawn and Garden WBC
100-784	2/97	4.5 lb/gal SC/L	D.Z.N. Diazinon AG600 WBC
100-785	11/96	4.5 lb/gal SC/L	D.Z.N. Diazinon Indoor/Outdoor WBC

[a] These products are registered for use in the home lawn and garden only and are therefore not summarized in Table A.

[b] Includes SLN No. CA810005.

A comprehensive summary of the registered food/feed use patterns of diazinon based on the above labels has been presented in the revised Residue Chemistry Chapter dated 12/1/00 (D.Drew, D270422). The conclusions regarding reregistration eligibility of diazinon for the crops listed in this chapter are based on the use patterns registered by the basic producer, Novartis, and summarized in the tolerance reassessment summary of this document. All end-use product labels (e.g., MAI labels, SLNs, and products subject to generic data exemption) must be amended such that they are consistent with the basic producer labels. (Guideline 860.1200).

(i). Nature of the Residue in Plants and Animals

The qualitative nature of the residue in plants is adequately understood pending review of confirmatory data from existing lettuce and green bean metabolism studies. Acceptable metabolism studies are available on sweet corn and potato. The HED Metabolism Assessment Review Committee (MARC) has determined that the residues of concern in plants and animals are diazinon, hydroxy diazinon, and diazoxon. For enforcement purposes, diazinon, per se will be included in the tolerance expression. However, the MARC recommended that residues of diazinon, and its metabolites, hydroxy diazinon and diazoxon, should be included in dietary risk assessment if they are found to be present or their concentration levels could be estimated for foods. Both of these metabolites are considered to be cholinesterase inhibitors. Residue data for plant and animal commodities should include analyses for all three compounds.

Based on a review of plant metabolism studies for apples, lettuce, corn, potatoes, and green beans, no residues of diazoxon or hydroxy diazinon were identified in either organic or aqueous fractions. All of the diazinon metabolites were identified as pyrimidine compounds or glucose conjugates of these compounds. Neither of these metabolites or their conjugates contain the cholinesterase inhibiting moiety. Consequently, they are not considered to be of significant toxicological concern for cholinesterase inhibition.

The qualitative nature of the residue in animals is adequately understood based upon acceptable poultry and ruminant metabolism studies. The HED Metabolism Committee has determined that the residues of concern in animals are diazinon, hydroxy diazinon, and diazoxon. For enforcement purposes, diazinon, per se, will be included in the tolerance expression. However, residues of diazinon, and its metabolites, hydroxy diazinon and diazoxon, should be included in dietary risk assessment if they are found to be present or their concentration levels could be estimated for foods. Both of these metabolites are considered to be cholinesterase inhibitors. Residue data for animal commodities should include analyses for all three compounds.

(ii). Analytical Methods

Adequate analytical methodology is available for data collection and enforcing tolerances of diazinon. Ciba-Geigy Method AG-550 (along with modifications) is a GC/FPD method that adequately recovers diazinon, diazoxon, and hydroxydiazinon from plant and animal matrices, and is the registrant's proposed enforcement method. As this method is essentially a modification of the Luke multiresidue method, independent laboratory validation may not be required pending radiovalidation with samples from the metabolism studies.

The FDA PESTDATA database dated 1/94 (PAM, Vol. I, Appendix I) indicates diazinon is completely recovered using FDA Multiresidue Protocols D and E (PAM, Vol. I Sections 232.4 and 311.1/212.2). Diazoxon and hydroxy diazinon are also completely recovered using Protocol D.

(iii). Storage Stability

Storage stability data are available indicating that diazinon and hydroxydiazinon are stable in/on frozen raw agricultural commodities (RACs) for up to 26 months. Diazoxon is not stable (<3 months). The registrant intends to conduct storage stability testing on residues in processed commodities, meat, and milk. However, the registrant may wish to note that tolerances for residues of diazinon in cattle, meat, meat byproducts, and fat, *except for the meat, meat byproducts and fat of sheep and the fat of beef,* are being recommended for revocation based on a determination that category 180.6(a)3 applies to these commodities, and that the establishment of a tolerance for milk is not warranted. Also additional stability studies are also being conducted on diazoxon and hydroxydiazinon to support special studies underway to determine the dissipation of diazoxon in fresh produce.

(iv). Residues in Raw Agricultural Commodities and Processed Food/Feed

Data requirements for magnitude of the residue of diazinon in plants for most raw agricultural commodities have been evaluated and deemed adequate to reassess diazinon tolerances. However, additional residue data are required for beans (lima), blueberries, celery, cucumbers, hops, dried peas (IR-4), spinach, sugar beets, and Swiss chard. Tolerances for these commodities will be reassessed once the required data have been submitted and reviewed. Because some of these commodities are representative crops (*) necessary for the establishment of crop group tolerances, crop group tolerances for the following crop groups are dependent on the submission and review of these data: Crop Group (2) Leaves of Root and Tuber Vegetables to cover turnips, sugar beets*, parsnips, carrots, radish, rutabaga, garden beets, and chicory. Crop Group (4) Leafy Vegetables to cover spinach*, parsley, celery*, Swiss chard*, dandelion, lettuce, and endive. Crop Group (9) to cover Cucurbit Vegetables to cover cucumber*, melons, and squash.

For purposes of reregistration, requirements for magnitude of the residue in plants are fulfilled for the following crops: almonds (California use only), apples, beans (snap), brassica leafy vegetables, blackberries, boysenberries, carrots, cherries, corn (sweet), cranberries, figs, grapes, kiwi fruits (tolerance import only), mushrooms, nectarines, peaches, peas (succulent), peppers, plums, onions (Crop Group 3, Bulb Vegetables) , pears, peppers (bell), pineapples, potatoes, radish/Chinese radish, squash, strawberries, tomatoes, turnips (roots and tops), walnuts (California use only), and watercress. Adequate field trial data depicting diazinon residues following applications made according to the maximum or proposed use patterns have been submitted for these crops. Geographical representation is adequate and a sufficient number of trials reflecting representative formulation classes were conducted.

IR-4 submitted data to support reassessed tolerances for figs (MRID 44726801) and watercress (MRID 44237101). The tolerance for figs has been reassessed based on the submitted residue data. The registrant can reinstate watercress on the labels or Hawaii can apply for a 24(c) Special Local Need (SLN) for watercress. IR-4 is supporting uses on filberts. They have generated residue field trial data; once these data have been submitted and reviewed, the tolerance for filberts can be reassessed.

Additional data are to be submitted on beans (lima), blueberries, celery, cucumbers, hops, peas (dried), spinach, sugar beets (roots and tops), and Swiss chard. Once residue data on these representative crops has been received and reviewed, sufficient data should be available to support tolerance reassessment for the crops listed above and the following crops: beet tops (garden), chicory, endive, melons, parsley, and squash. Alternatively, once the residue data for the above-listed crops has been submitted and reviewed, if any interested party wishes to support additional crop uses within a crop grouping, sufficient residue data should be available to support crop group tolerances.

The registrant is not supporting uses on the following crops for which tolerances are established: alfalfa, bananas, citrus fruits, clover, coffee, cottonseed, figs, filberts, grasses, olives, peanuts, pecans, sorghum, soybeans, or sugarcane. The Agency is proposing to revoke tolerances for beans, guar, cowpeas, olives, peanuts, pecans, soybeans, and sugarcane. IR-4 has submitted residue data to support uses on figs, and has expressed interest and generated residue data in support of uses on filberts as noted above. Once it has been determined that no other interested party wishes to support the remaining uses for alfalfa, bananas, citrus fruits, clover, coffee, cottonseed, and grasses these tolerances should be revoked as well.

The reregistration requirements for magnitude of the residue in processed food/feed commodities are fulfilled for apple, figs, grapes, pineapples, plums, potatoes, sugar beets, and tomatoes. Residues of diazinon did not concentrate in plant processed commodities except for dried figs (6X). Preliminary data indicate that residues of diazinon may concentrate in dried sugar beet pulp (2X); however, additional residue data on sugar beets reflecting current label rates and PHI are necessary to determine if feed additive tolerances are necessary. Once the residue data are received and reviewed a tolerance may need to be established for sugar beet pulp based on the concentration factor and the highest average field trial (HAFT) residue for sugar beets. A tolerance should be established on dried figs at 0.3 ppm as per the HED Residue Chemistry chapter.

Regarding the magnitude of the residue for the diazoxon and hydroxy diazinon metabolites, a review of residue field trial data for 25 crops and approximately 2000 samples analyzed for diazoxon and hydroxy diazinon indicated the following: for samples treated at the equivalent of currently-labeled 1X application rates and harvested at the currently-labeled post-harvest intervals (PHIs), all samples showed non-detectable residues (<0.01 ppm) for all crops, except for celery, spinach, and peppers. Hydroxy diazinon was detected in celery after a 1X pre-plant, soil-incorporated application combined with a 1X foliar application up to the post-harvest interval (PHI). Current label rates for celery no longer include the foliar applications close to the time of harvest, but do include a pre-plant, soil-incorporated application. It is anticipated that the new use pattern, may lower detectable residues on harvested celery. Diazoxon and hydroxy diazinon residues were detected in spinach at 2% and 1% of the parent compound, respectively. Hydroxy diazinon was detected in peppers at low levels above the detection limit (0.07 ppm) approximately 27% of the parent compound. Foliar application rates for peppers have been lowered 3-fold (3X) from 3.75 lbs ai/A/season to 1.25 lbs ai/A/season on current labels, and the PHI used in the study was 3 days versus the currently-labeled 5 days. It is anticipated that the new use pattern may lower residues on peppers. The summary data for these 3 crops indicated that 1 spinach sample and 4 pepper samples contained detectable metabolite residues. It was unclear how many celery samples (1 or more) were positive for the hydroxy diazinon metabolite.

(v). Residues in Meat, Milk, Poultry, and Eggs

Poultry. Finite residues of diazinon, and its two cholinesterase inhibiting metabolites are not expected in poultry or eggs as a result of residues of diazinon on poultry feed items. A 40 CFR §180.6(a)(3) condition exists and tolerances for poultry tissues and eggs will not be required. A poultry feeding study has been deemed adequate for diazinon, diazoxon, and hydroxydiazinon pending the submission of supporting storage stability data.

Ruminant. Many of the feed items originally used to estimate secondary residues of diazinon in livestock commodities are no longer supported or have been determined not to be significant livestock feed items. As a result of this and a reassessment of existing tolerances for diazinon on ruminant feed items, the maximum theoretical dietary burden for diazinon in ruminants has been revised and is presented below. The theoretical 1X feeding level has been recalculated as 11 ppm and 13 ppm, respectively for dairy and beef cattle. A ruminant feeding study (reviewed and deemed adequate for diazinon, diazoxon, and hydroxy diazinon to support reregistration of diazinon) was conducted at 3 times (40 ppm) to 36 times (400 ppm) these theoretical maximum dietary burden rates. Extrapolating from residues detected at these exaggerated feeding levels to anticipated residues at the maximum theoretical dietary burdens indicate that a 40 CFR §180.6(a)(3) condition may exist, and there is no expectation of finite residues of diazinon or its cholinesterase inhibiting metabolites for cattle tissues and milk as a result of residues on livestock feed items.

The calculated maximum theoretical dietary burdens for livestock are presented below (note that sugar beet tops are not fed to dairy cattle):

Feed Commodity	% Dry Matter [a]	% Diet [a]	Reassessed Tolerance (ppm)	Dietary Contribution (ppm) [d]
Beef Cattle				
Almonds, hulls	90	10	3.0	0.33
Corn forage	48	40	10.0	8.3
Sugar beet pulp	88	20	1.0	0.28
Sugar beet tops	23	10	10.0	4.3
Other	--	20	0	0
TOTAL BURDEN		100		13.3
Dairy Cattle				
Almonds, hulls	90	10	3.0	0.33
Corn forage	48	50	10.0	10.4
Sugar beet pulp	88	20	1.0	0.28
Other	--	20		0
TOTAL BURDEN		100		11.0

[a] Table 1 (August 1996).

[b] Contribution =[(Reassessed tolerance / fraction DM) X fraction diet].

Summaries of existing studies measuring the magnitude of diazinon residues in sheep tissues after spray applications were considered in reassessing tolerances for sheep tissues required for the use of diazinon on sheep. Results from those studies indicate that existing tolerances of 0.7 ppm in sheep tissues (meat and meat byproducts) are adequate; however, the existing tolerance for diazinon in sheep, fat, should be raised from 0.7 ppm to 5.0 ppm.

Based on cattle ear tag study results, the diazinon tolerance for the fat of beef should be decreased from 0.7 ppm to 0.5 ppm. The tolerance for beef meat and meat by-products (mbyp) can be revoked as there is "no reasonable expectation of finite residues" {Category 180.6(a)3} on cattle meat and mbyp from registered uses of cattle ear tags or from the consumption of diazinon treated feed items by cattle. A diazinon tolerance for milk is not required as long as the ear tag labels maintain that use is for beef cattle and *non-lactating* dairy cattle, only.

(vi). Residues in Water, Fish, and Irrigated Crops

The labels listing uses on cranberries have been revised to include a restriction against using water from irrigated or flooded cranberry bogs or watercress beds to irrigate other crops (except other crops with registered diazinon uses) or for drinking purposes:

"Do not use water from irrigated or flooded cranberry beds for drinking purposes or to irrigate crops other than those appearing on EPA Approved Diazinon labels".

This language should be added to the following existing 24(c) labels specific to cranberry uses: OR900017 and WA900027 (Gowan), WA970001, WI980003, NJ970001, OR970002, and MA970001 (Palette), and WI880009 (Wilber Ellis).

Given this label restriction, OPPTS GLN 860.1400 does not apply to diazinon.

(vii). Residues in Food/Feed Handling Establishments

Labeled uses of diazinon in food and feed handling establishments are listed on the diazinon 4E label. Adequate data are available reflecting the use of diazinon in food handling establishments. The data reviewed in the Reregistration Standard Update indicate that tolerances of 0.02 ppm (2 X the limit of quantitation for the method to account for diazinon and metabolites) should be established for residues in food and feed resulting from use of diazinon in food and feed handling establishments based on non-detectable residues of diazinon, hydroxy diazinon, and diazoxon at 1X and 2X use rates. Labels require that diazinon be applied as a limited spot treatment or a crack and crevice treatment only. Foods must be removed and/or covered during application. Based on data submitted to support the food additive petition (180.153(a)(2) & (3)) and associated label restrictions on commercial applicators applying diazinon in food/feed handling establishments, there is no likelihood of detectable residues [Limit of Detection (LOD) is 0.01 ppm] on food/feed provided label directions are followed.

Although the establishment of a tolerance is necessary because use in food/feed handling establishments is considered a food use, it is not necessary to include this use in the dietary risk assessment. Because residues were non-detectable (<0.01 ppm) for diazinon, hydroxy diazinon, and diazoxon as a result of a 1X and 2X labeled application rate in food/feed handling establishments, it is recommended that the dietary risk assessment for diazinon be conducted including potential residues from the food/feed handling establishment use at ¼ the limit of detection (0.0025 ppm or ½ LOD extrapolated to 1x use rate) for diazinon, hydroxy diazinon, and diazoxon, each, and assuming the non-detectable residues are zero (as per TRAC Science Policy paper entitled, “Assigning Values to Nondetected/Nonquantified Pesticide Residues in Human Health Dietary Exposure Assessments”, draft 11/30/98).

(viii). Confined Accumulation in Rotational Crops

An adequate confined rotational crop study is available. These data indicate that residues of diazinon in rotational crops are qualitatively similar to the residues resulting from the direct application of diazinon to the primary crops. Based on the results of this study, limited field rotational crop studies on three representative crops are required.

(ix). Anticipated Residues and/or Monitoring Data and Percent Crop-Treated

HED's current dietary exposure assessment for diazinon is provided below under section b. Dietary Risk Characterization - Food Sources. Specific anticipated residues used for each food commodity included in this assessment are provided in the memo, Diazinon: Acute and Chronic Dietary Risk Assessment but are described briefly here. The anticipated residues in this assessment are based on the following sources, in order of preference: USDA PDP monitoring data, FDA surveillance monitoring data, and controlled field trial data. The monitoring data are preferred over field trial data because samples are more reflective of residues that may occur on foods as consumed. The PDP data are preferred because, in general, more samples are taken, and the sampling protocols have been designed to reflect variations in consumption patterns throughout the year and geographically. PDP samples include both domestic and imported foods.

The USDA Pesticide Data Program (PDP) has surveyed pesticide residues in selected food items since 1991. Final data are available for diazinon up through 1997. In this assessment we have considered these final data, as well as, preliminary data from the years 1998 and 1999. The PDP program has reported analyses for diazinon *per se* for almost all commodities up through 1998. The preliminary 1999 data include analyses for the diazoxon for single servings of apples, as well as, composited samples of apples, peppers, spinach, strawberries, and tomatoes. For the 1997 data, out of 11 crops and more than 7000 samples analyzed, no detectable diazoxon residues were reported with the exception of 1 spinach sample that contained residues at 50% of the parent compound. Although not normally included in the analyses, an unidentified chromatogram peak was investigated on 1 spinach sample and was determined to be the oxon of diazinon. The preliminary 1998-1999 data on 5 crops (apples, peppers, spinach, strawberries, and tomatoes) show no detectable diazoxon residues in any of the more than 1400 samples analyzed. FDA monitoring data for diazinon and the hydroxy and oxon metabolites of concern were considered for the years 1992 through 1998. There were no reports of detectable residues of the metabolites of diazinon for these years either in domestic or imported foods.

The HED MARC suggested including diazoxon and hydroxy diazinon in dietary risk assessments if they were found to be present or if their concentration levels could be estimated in foods. However, based on the above PDP and FDA monitoring data, a review of field trial data in which detections of either metabolite were sporadic (see section (3)(a)(i)), and results from 5 metabolism studies in which neither hydroxy diazinon nor diazoxon were found (see section (3)(a)(iv)), concentrations of these 2 metabolites were assumed to be zero in the dietary assessments. The preponderance of residue data from metabolism studies, residue field trials and monitoring data (USDA's PDP and FDA Surveillance Monitoring data) indicate that these two metabolites are infrequently to never detected for the majority of crops analyzed for diazoxon and hydroxy diazinon. If there is a concern regarding how the metabolites were handled in the dietary assessments, HED could revise the current dietary assessments to include the residues of these compounds where warranted on a crop-specific basis, but there appears to be no cogent rationale for including these metabolites in all crops at some default value in light of the available residue data. HED does not recommend assuming ½ the limit of detection values for both metabolites across all crops. HED believes this would result in an overly conservative assessment driven by these default ½ LOD values because of the relatively low levels of diazinon, *per se*.

Residue data from PDP were decomposited for the following crops to obtain, initially, 1000 residue values, which were later truncated at the tolerances of their respective crops prior to incorporation into the acute dietary analysis: carrots, peaches, apples, celery and head lettuce. The residue values generated by decomposition were also extended (translated) to crops with unavailable or insufficient residue data. Accordingly, data for carrots were translated to turnip-roots, rutabagas, and parsnips; data for peaches were translated to apricots and nectarines, and data for celery were translated to Swiss chard. In cases where monitoring data were translated to similar commodities, this was done in accordance with guidance found in HED SOP 99.3 for Translation of Monitoring Data (March 26, 1999). For those cases in which field trial data were used, the anticipated residues were based on the maximum supported use patterns, as summarized in the RED. If neither adequate monitoring data or information on supported use patterns were available, then residues were assumed to be at the tolerance level (see Table 4).

Table 4. Diazinon: Translation of Pesticide Monitoring Data.

Commodity Analyzed	Source of Data	Commodity Translated to
Peach	PDP	Apricot, Nectarine

Table 4. Diazinon: Translation of Pesticide Monitoring Data.		
Commodity Analyzed	Source of Data	Commodity Translated to
Spinach	PDP	Garden Beet tops, Turnip tops, Parsley, Dandelion
Blackberry/Raspberry	FDA	Other Caneberries
Orange*	PDP	Other Citrus*
Orange Juice*	PDP	Other Citrus Juice*
Carrots	PDP	Parsnip, Rutabaga, Turnip root, Ginseng
Garden Beet Roots	FDA	Sugar Beets
Celery	PDP	Swiss Chard
Collards, Kale, Mustard Greens combined	FDA	Combined residue data used
Lettuce	PDP	Radicchio
Bok choy	FDA	Chinese broccoli
Broccoli	FDA	Brussels sprouts
Cauliflower	FDA	Kohlrabi
Green Onions	FDA	Leeks
Bulb Onions	FDA	Shallots, Garlic
Green Peppers	FDA	Other peppers Hot Peppers
Cantaloupe	FDA	Casaba, Crenshaw, Honeydew, Persian Melon, Balsam Pear, Bitter Melon,Wintermelon
Green Beans	PDP	All Succulent Beans, Succulent Blackeyed Peas
Bananas*	PDP	Plantain*
Radish and Oriental Radish combined	FDA	Oriental Radish
Wheat Grain	PDP	Sorghum

* Crops/commodities with an asterisk are no longer supported by the registrant. However, because these commodities have tolerances, they have been included in the dietary risk assessments. Once it has been determined that no other interested party wishes to support these uses, the tolerances can be recommended for revocation, and these commodities removed from the dietary assessments.

Percent Crop Treated Data

A quantitative usage analysis for diazinon was provided by BEAD based on data years 1987-96 (Alan Halvorson, QUA date: January 29, 1999 and October 6, 2000). Data sources included USDA/NASS (1990-97), California EPA, Department of Pesticide Regulation (1993-95), National Center for Food and Agricultural Policy, the USDA's Foreign Agricultural Service website (http://www.fas.usda.gov/dlp/beef/Beefpage.htr various proprietary data sources (1987-97). The weighted average of the percent of crop treated was used for estimating chronic dietary exposure and an estimated maximum of the percent of crop treated was used for estimating acute dietary exposure. Percent crop treated information was used either as a predictor of the probability of residues occurring on a given monitoring sample as in the acute dietary assessment or, as in the case of blended commodities and for chronic exposure, as an adjustment factor to the average residue occurring in a commodity. For some of the PDP commodities, imported samples comprise a significant portion of the database. For those commodities, the percent crop treated information provided by BEAD was adjusted to account for imports. The assumption was made that for those commodities consumed solely from imports, 100% of the crop had been treated. Similarly, for cattle and sheep dermal treatments, it was assummed that 100% of imported sheep and cattle are treated with diazinon. The risk assessment may be further refined once information on the percentage of imported crops and imported animal commodities treated with diazinon is made available.

Processing Factors

All processing factors used in this assessment are summarized in Table 5. These factors are input into the DEEM software as adjustment factor #1.

Table 5. Diazinon Processing Factors Summary

Category	Processing Factor used for current analysis	Data Sources	Comments and Agency Reviews
Apples-dried	8	DEEM Default	
Apples-juice/cider	1		Monitoring data used for juice
Apples-juice-concentrate	3	Ratio of Default factors for juice & concentrate	Conc. factor applied to juice

Table 5. Diazinon Processing Factors Summary			
Category	**Processing Factor used for current analysis**	**Data Sources**	**Comments and Agency Reviews**
			data
Apricots-dried	6	DEEM Default	
Bananas-dried*	3.9	DEEM Default	
Cherries-dried	4	DEEM Default	
Cherries-juice	1.5	DEEM Default	
Cottonseed meal*	0.44	MRID 00032881	S. Funk, 4/17/92 used average factor from all studies with detectable residues
Cottonseed Oil*	2.2	MRID 00032881	S. Funk, 4/17/92 used average factor from all studies with detectable residues
Cranberries-juice	1.1	DEEM Default	
Cranberries-juice-concentrate	3.3	DEEM Default	
Grapefruit-juice*	1		Used orange juice monitoring data
Grapefruit-juice-concentrate*	3.9	Ratio of Default factors for juice & concentrate	Factor applied to orange juice monitoring data
Grapes-juice	1	MRID 41410001	Monitoring data used for grape juice.
Grapes-juice-concentrate	3	Ratio of Default factors for juice & concentrate	
Grapes-raisins	0.13	MRID 41410001	S. Funk, 4/17/92 used average factor from all studies with detectable residues
Lemons-juice*	1		Used orange juice monitoring data

Table 5. Diazinon Processing Factors Summary			
Category	**Processing Factor used for current analysis**	**Data Sources**	**Comments and Agency Reviews**
Lemons-juice-concentrate*	5.7	Ratio of Default factors for juice & concentrate	Factor applied to orange juice monitoring data
Limes-juice*	1		Used orange juice monitoring data
Limes-juice-concentrate*	3	Ratio of Default factors for juice & concentrate	Factor applied to orange juice monitoring data
Onions-dehydrated or dried	9	DEEM Default	
Oranges-juice*	1		Used orange juice monitoring data
Oranges-juice-concentrate*	3.7	Ratio of Default factors for juice & concentrate	Factor applied to orange juice monitoring data
Peaches-dried	7	DEEM Default	
Pears-dried	6.25	DEEM Default	
Pineapples-dried	5	DEEM Default	
Pineapples-juice	0.12	MRID 42179501	P. Deschamp, 6/3/92, D174774
Pineapples-juice-concentrate	0.44	MRID 42179501	(juice factor) *(ratio of DEEM defaults for juice & concentrate)
Plantains-dried	3.9	DEEM Default	
Plums/prunes-juice	1.4	DEEM Default	
Plums/prunes-dried	0.6	MRID 43274401	S. Funk, 5/24/93,D189573
Potatoes/white-dry	6.5	DEEM Default	
Sugar-beet-molasses	0.5	MRID 41336514	Diazinon Reg. Std. Update, 1/24/92
Tangerines-juice*	1		Used orange juice monitoring data
Tangerines-juice-concentrate*	3.2	Ratio of Default factors for juice & concentrate	Factor applied to orange juice monitoring data

Table 5. Diazinon Processing Factors Summary			
Category	**Processing Factor used for current analysis**	**Data Sources**	**Comments and Agency Reviews**
Tomatoes-catsup	0.30	MRID 41336508	S. Funk, 4/17/92 used average factor from all studies with detectable residues
Tomatoes-dried	14.3	DEEM Default	
Tomatoes-juice	0.05	MRID 41336508	S. Funk, 4/17/92 used average factor from all studies with detectable residues
Tomatoes-paste	0.60	MRID 41336508	S. Funk, 4/17/92 used average factor from all studies with detectable residues
Tomatoes-puree	0.70	MRID 41336508	S. Funk, 4/17/92 used average factor from all studies with detectable residues

* Crops/commodities with an asterisk are no longer supported by the registrant. However, because these commodities have tolerances, they have been included in the dietary risk assessments. Once it has been determined that no other interested party wishes to support these uses, the tolerances can be recommended for revocation, and these commodities removed from the dietary assessments.

Dietary exposure assessment

The following commodities, for which all uses have been canceled and tolerance revocations have been recommended, are not included in the current assessment:

- olives
- peanuts
- pecans
- soybeans
- sugarcane
- beans, guar
- cowpeas

The potential for transfer of residues to meat, milk, poultry and eggs from animal feeds has been reassessed. It has been determined that measurable secondary residues in these tissues are not likely as a result of diazinon residues in animal feed items. Dermal treatments are not being supported for any livestock or poultry except sheep and cattle. Therefore, the following commodities <u>are not included</u> in the current assessment:

- milk
- all poultry meats and meat byproducts
- eggs
- livestock meats and meat byproducts <u>except for the meat, meat byproducts and fat of sheep and the fat of beef</u>

Uses of diazinon on the following crops are not being supported by the registrant; however, they <u>are included</u> in the present assessment because of their existing tolerances and pending a determination of whether any other interested party wishes to support them.

- citrus fruits
- coffee
- cotton
- bananas
- sorghum

Tolerance level residues were assumed to be present in coffee and cottonseed. The registrant is not supporting uses on alfalfa but tolerances are established for forage (40 ppm) and hay (10 ppm). The only alfalfa food commodity is alfalfa sprouts. This commodity is not being considered in the present assessment because, in our judgement, there is little likelihood for use of diazinon on alfalfa grown for sprouts or from dietary exposure to diazinon via consumption of sprouts.

Anticipated residues were derived in accordance with established Agency policies and guidance for chronic and acute dietary exposure assessments. Residues for chronic analysis are generally based on the mean of the best available residue data with appropriate adjustments for percent crop treated and residue concentration/reduction from processing. Acute anticipated residues were derived using guidance provided in HED SOP 99.6 (Classification of Food Forms with Respect to Level of Blending (8/20/99)). Each food form entered in the DEEM software for dietary exposure assessments is classified as being blended (B), partially blended (PB), or not blended (NB). As more extensively described in the SOP, PDP, and FDA monitoring data, which are generally based on composite samples, may be used to construct residue distributions for input into a Monte Carlo analysis using the DEEM software. If foods are blended (B or PB) the entire distribution of monitoring data can be used to represent a distribution. If the foods are classified as not blended (NB) then further evaluation of PDP and FDA data are required before compiling a residue distribution. The composited samples from PDP and FDA (5 to 20 lbs) may not reflect residue levels in single-serving commodities. Thus, these monitoring data should be "decomposited" via a suitable statistical procedure in order to simulate a distribution of single serving commodities. In the current analysis, we are using a procedure developed by HED (Allender, H. "Use of the Pesticide Data Program (PDP) in Acute Dietary Assessment," EPA interim guidelines, August 1998). At present our decompositing procedure requires that the available monitoring data contain at least 30 detects. If fewer than 30 detects occur then a judgement is made as to whether the composite data set may be used either directly or with an appropriate multiplication factor. These considerations are also discussed at length in HED SOP 99.6. In the current assessment, we have applied some criteria to using the available composite monitoring data for foods that are not blended. The criteria and assumptions involved are as follows:

- Any tolerance-exceeding residues in the monitoring data are considered to exist because of off-label uses, and are excluded from the anticipated residues, which are intended to represent good agricultural practices.

- If monitoring data for a not-blended food contain enough detectable residues (~30 or more), then the data are decomposited with the Allender method. This method produces a lognormal distribution of residue values that is used in a Monte Carlo analysis.

- The lognormal distribution obtained by the Allender method is truncated at the tolerance level for the commodity of interest. Although tolerances are also based on composite samples, these are from controlled field trials in which it is assumed that all components of the composite have been treated with the maximum allowable level of diazinon. Therefore, it is assumed that the tolerance, which is based on a rounded up maximum residue value from field trials, would not be exceeded in single servings, if good agricultural practices are followed.

- If significantly fewer than 30 detectable residues occur in the monitoring data, then the Allender method is not used. If the monitoring data contain very low residues then they are used directly with the assumption that residue levels could not be underestimated significantly. If some of the residues are significantly higher than the LOD of the analytical method, then a multiplication factor is applied to the detected residues as a conservative simulation of residues that may occur in single servings within a given composite sample. This factor is derived as follows: The tolerance for the commodity of interest is divided by the highest residue level reported. All detects for that commodity are multiplied by this factor and the adjusted data are used directly to construct a residue distribution for Monte Carlo analysis.

(x.) Consumption Data

The acute and chronic module version 7.075 of DEEM™ were used for these exposure assessments. Consumption of the various commodities was estimated from the 1989 - 1992 USDA *Continuing*

Surveys of Food Intake for Individuals.

b. Dietary Risk Characterization - Food Sources

(i). Acute Dietary (Food) Exposure and Risk Estimates

The estimate of acute dietary exposure from uses of diazinon on food/feed crops and animals is summarized in Table 6. The DEEM inputs and complete acute dietary analysis are presented in (D269781, 11/14/00, D.Drew). As per OPP policy, a reference dose (RfD) modified by an FQPA safety factor is referred to as an population-adjusted dose (PAD). Because the FQPA safety factor was reduced to 1x for diazinon, the acute RfD is equal to the acute PAD. The acute PAD for diazinon is 0.0025 mg/kg. For the groups listed in Table 6, the estimated acute risks at the 99.9th percentile of exposure ranged from 23% of the aPAD for males 13 to 19 years old to 63% of the aPAD for the most highly-exposed subgroup, children 1 to 6 years old. Risk estimates for all subgroups analyzed were less than 100% of the aPAD and therefore risk estimates for the U.S. population and all subgroups are below HED's level of concern.

Table 6. Acute Dietary Exposure Results for Diazinon Including Sheep Commodities and Beef Fat

Total Exposure by Population Subgroup				
Population Subgroup	Total Exposure @ 99th Percentile		Total Exposure @ 99.9th Percentile	
	mg/kg body wt/day	Percent of aPAD	mg/kg body wt/day	Percent of aPAD
U.S. Population (total)	0.000294	12	0.000936	37
All infants (< 1 year)	0.000321	13	0.000724	29
Children 1-6 yrs	0.000530	21	0.001577	63
Children 7-12 yrs	0.000330	13	0.000789	32

Table 6. Acute Dietary Exposure Results for Diazinon Including Sheep Commodities and Beef Fat				
Total Exposure by Population Subgroup				
Population Subgroup	Total Exposure @ 99th Percentile		Total Exposure @ 99.9th Percentile	
	mg/kg body wt/day	Percent of aPAD	mg/kg body wt/day	Percent of aPAD
Females 13-50 yrs	0.000229	9.2	0.000882	35
Males 13-19 yrs	0.000254	10	0.000587	23
Males 20+ yrs	0.000262	10	0.000918	37
Seniors 55+	0.000253	10	0.000895	36

aPAD = 0.0025 mg/kg

Critical Commodity Analysis

An analysis of commodities contributing most highly to acute dietary exposure to diazinon for the most highly exposed subgroup indicated that beef fat and sheep commodities (fat and lean meat) were the major contributors to high exposure events in the Monte Carlo analysis. It should be noted that the anticipated residues for these commodities are conservative. The maximum reported residues in sheep and beef tissues from dermal uses were used in the dietary analyses. The maximum residue value for sheep fat (2.2 ppm), and sheep lean lean meat (0.13 ppm) have been adjusted for percent of sheep consumed treated with diazinon sprays (37%). The residue values for sheep were obtained from studies where sheep were "dipped", or submerged, which is not a label use. The maximum value for beef fat (0.39ppm) was adjusted for percent beef fat consumed from cattle treated with ear tags (14%). However, these values are not considered to be highly refined, but were the best available. The percentage used for treated sheep consumed reflects partial knowledge of the percentage of domestic sheep consumed (65%) and the number of domestic sheep treated with diazinon (3%), and the percentage of imported sheep consumed (35%) and the assumption that all imported sheep are treated with diazinon (100%). Similarly, the percentage used for treated beef consumed reflects partial knowledge of the percentage of domestic beef consumed (89%) and the maximum percent of domestic cattle treated with diazinon (4%), and the percentage of imported beef consumed (11%) and the assumption that all imported beef is treated with diazinon (100%). HED notes that the assumption that100% of imported sheep and 100% of imported beef are treated with diazinon is likely to be conservative and may overestimate the resultant exposures. Further refinements to the estimates of sheep and cattle treated with diazinon, domestic and imported, would refine dietary risk estimates.

When sheep and beef are removed from the analyses the acute exposures and resulting risk estimates decreased for all groups, most notably for children 1-6 yrs where the risk estimate at the 99.9th percentile dropped from 63 % aPAD to 47% aPAD. These results are summarized below in Table 7.

Table 7. Acute Dietary Exposure Results for Diazinon Excluding Sheep and Beef Commodities.

Total Exposure by Population Subgroup		
Population Subgroup	Total Exposure @ 99.9th Percentile	
	mg/kg body wt/day	Percent of aPAD
U.S. Population (total)	0.000660	26
All infants (< 1 year)	0.000658	26
Children 1-6 yrs	0.001187	47
Children 7-12 yrs	0.000597	24
Females 13-50 yrs	0.000603	24
Males 13-19 yrs	0.000516	21
Males 20+ yrs	0.000545	22
Seniors 55+	0.000691	28

(ii). Chronic Dietary (Food) Exposure and Risk Estimates

As per OPP policy, a reference dose (RfD) modified by an FQPA safety factor is referred to as a population-adjusted dose (PAD). Because the FQPA safety factor was removed for diazinon, the chronic RfD is equal to the chronic PAD (cPAD). The cPAD for diazinon is 0.0002 mg’kg/day. For the groups listed in Table 8, the estimated chronic risks ranged from 10% of the cPAD for males 13- 19 years to

22% of the aPAD for the most highly-exposed subgroup, children 1 to 6 years old. Risk estimates for all subgroups analyzed were less than 100% of the cPAD and therefore risk estimates for all subgroups are below HED's level of concern. The dietary exposure model inputs and complete chronic analysis are presented in the memorandum of 11/14/00 (D269781, D.Drew). For the most-highly exposed subgroup (children 1-6 years) the major contributor to the estimated exposure was beef fat.

Table 8. Chronic Dietary Exposure Results for Diazinon Including Sheep Commodities and Beef Fat		
Total Exposure by Population Subgroup		
Population Subgroup	Total Exposure	
	mg/kg body wt/day	Percent of cPAD
U.S. Population (total)	0.000028	14
All infants (< 1 year)	0.000023	12
Children 1-6 yrs	0.000045	22
Children 7-12 yrs	0.000029	14
Females 13-50 yrs	0.000024	12
Males 13-19 yrs	0.000020	10
Males 20+ yrs	0.000027	14
Seniors 55+	0.000028	14

cPAD = 0.0002 mg/kg/day

Critical Commodity Analysis

An analysis of commodities contributing to the chronic dietary exposure to diazinon for the most highly exposed subgroup, children 1-6 years, indicated that beef fat was the major contributor to high exposure events in the analysis. As noted in the above acute critical commodity discussion, the anticipated residue for beef fat is conservative. The maximum reported residue in beef fat from cattle ear tag use at the maximum application rate was used in the dietary analyses. Also assumed was the percentage of domestic beef consumed (89%) and the percent (weighted average) of domestic cattle treated with diazinon (1.5%), and the percentage of imported beef consumed (11%) . It was assumed that all imported beef is treated with diazinon (100% treated). HED reiterates that the assumptions, especially that 100% of imported beef are treated with diazinon , are likely to be conservative and may overestimate the resultant exposures. Further refinements to the estimates of cattle treated with diazinon, domestic and imported, would refine the dietary risk estimates.

When beef fat and sheep commodities are removed from the analyses the chronic exposures and resulting risk estimates decreased for all groups (all risk estimates #13% of the cPAD). These results are summarized below in Table 9.

Table 9. Chronic Dietary Exposure Results for Diazinon Excluding Sheep and Beef Commodities		
Total Exposure by Population Subgroup		
Population Subgroup	Total Exposure	
	mg/kg body wt/day	Percent of cPAD
U.S. Population (total)	0.000018	8.9
All infants (< 1 year)	0.000019	9.5
Children 1-6 yrs	0.000025	13
Children 7-12 yrs	0.000016	7.8
Females 13-50 yrs	0.000017	8.3
Males 13-19 yrs	0.000008	4.1
Males 20+ yrs	0.000017	8.7
Seniors 55+	0.000023	11

Food Handling Establishment Uses

Diazinon food handling establishment tolerances are being recommended; therefore, a discussion of the dietary risk from such uses is included. These uses could have been included in the chronic dietary assessment; however, there is little basis for conducting such an assessment other than exercising a judgement based on knowledge of the properties of diazinon and the nature of its uses in food handling areas. The use directions on diazinon labels are very detailed and designed to avoid any contact with foods. HED concludes with respect to food/feed handling establishment uses that it is unlikely that any residues of diazinon will occur on foods from these uses as long as it is used according to the label. Nevertheless, HED conducted a chronic dietary exposure and risk analysis which included food/feed handling establishment uses and may be useful for approximating a worst-case scenario. The only quantitative data available for such an assessment is a residue study conducted at twice the label rate in a food handling establishment. Residues were non-detectable (<0.01 ppm) on a variety of foods exposed in this test.

For the purposes of a very conservative assessment, a residue on 100% of exposed food was assumed to be 0.0025 ppm (½ LOD extrapolated to 1x use rate or ¼ of the LOD). No information on what percent of food handling establishments may actually be treated with diazinon was available, so the assumption was made that all food consumed comes from treated establishments. The value of 0.0025 ppm was input into all food forms, except water, in a dietary analysis, and all default concentration factors were removed. The results ranged from a low of 0.000034 mg/kg body wt/day (17% of cPAD) for females over 20 years (not pregnant or nursing) to a high of 0.000142 mg/kg body wt/day (71% of cPAD) for children between 1 and 6 years old. The exposure for the total U. S. Population was 0.000051 mg/kg body wt/day (26% of cPAD). As can be deduced from the results of this exercise, exposure to diazinon accounts for less than 100% of the cPAD (71% of cPAD for food-handling uses plus 13% of cPAD for the remaining dietary exposures for children 1 to 6) even with residues included in the chronic dietary assessment at 0.0025 ppm (1/4 LOD) for all foods to cover food-handling establishment uses. However, in order to estimate a reasonable, worst-case exposure from this exercise, one needs much more data than currently available. The actual usage of diazinon in all types of food handling establishments (the percentage of establishments receiving diazinon treatments) would have to be considered at the least.

c. Dietary Exposure - Drinking Water

The EPA's Office of Water has established an adult lifetime Health Advisory (HAL) for diazinon of 0.6 ug/L, but at this time has not established a Maximum Contaminant Level (MCL). Environmental fate data indicate that diazinon may occur in both ground water and surface waters to varying degrees. Diazinon is only moderately mobile and persistent. Laboratory data indicate that diazinon will not persist in acidic water; however, in neutral and alkaline waters, residues may be quite persistent. Oxypyrimidine is the main soil and water degradate. Diazoxon, a toxic degradate, was not found in laboratory fate studies but was found in the field dissipation studies. To date, ground and surface water monitoring studies have not analyzed for oxypyrimidine or diazoxon. Previously, the HED Metabolism Assessment Review Committee (MARC) concluded that focusing on diazinon, *per se*, in water should be adequate for the purposes of risk assessment. This decision included consideration of the likelihood of occurrence in water of major soil and water metabolites that are toxicologically significant (HED MARC memorandum from D. Hrdy to G. Kramer dated 4/17/98). However, a recent literature study indicates that diazinon is converted to diazoxon during drinking water treatment by chlorination and that it may persist for up to 48 hours in finished water (see revised EFED chapter of 11/00).

Currently, HED uses drinking water levels of comparison (DWLOCs) as a surrogate to capture risk associated with exposure to pesticides in drinking water in accordance with HED SOP 99.5. A DWLOC is the concentration of a pesticide in drinking water that would be acceptable as a theoretical upper limit in light of total aggregate exposure to that pesticide from food, water, and residential uses (if any). It is used as a point of comparison against the model estimates to determine if the estimated concentration is of concern. A DWLOC may vary with drinking water consumption patterns and body weights for specific subpopulations. To calculate the DWLOC for acute exposure relative to an acute toxicity endpoint, the acute dietary food exposure (from the DEEM™ analysis) was subtracted from the acute PAD to obtain the acceptable acute exposure to diazinon in drinking water. To calculate the DWLOC for chronic (non-cancer) exposure relative to a chronic toxicity endpoint, the chronic dietary food exposure (from DEEM™) plus any potential chronic residential exposures was subtracted from the chronic PAD to obtain the acceptable chronic (non-cancer) exposure to diazinon in drinking water. DWLOC values were calculated using default body weights and consumption values (70 kg for adult males, 60 kg for adult females, and 10 kg for children, and drinking water consumption figures of 2 L/day for adults and 1 L/day for children). A comparison of DWLOC values for acute and chronic risk to estimated concentrations of diazinon in ground and surface waters is given in Tables 20 and 21 below. Example DWLOC calculations are also provided in the section below.

i. Groundwater (modeling/monitoring)

EFED summarized the results from a variety of ground water monitoring studies that included diazinon as an analyte. No metabolites were included in the analyses. The results of some of these studies are briefly outlined here. For a full discussion of the water quality data used, please see EFED memorandum dated 11/00 for complete details. In general, diazinon has been detected in ground water from a variety of sources, drinking water wells, monitoring wells, and agricultural wells. Many of the studies conducted have been located in areas where pesticide use and agricultural production are considered to be high. However, the studies have not been targeted explicitly to diazinon use patterns. Summary statistics were included for each sampling study conducted. For each study, range, mean, median, and 95th percentile values were determined from all samples analyzed including non-detects which were given a value of ½ the limit of detection. Based on the data presented in the EFED memorandum, the concentrations of diazinon detected in ground water (all wells) ranged from non-detectable (ND) to 1.0 ug/L.

Much of the groundwater data provided comes from the USGS National Water Quality Assessment Program (NAWQA), which assesses ambient water quality. Approximately 2% of the groundwater samples collected through this program from 1992 to 1996 had positive detections of diazinon. The maximum concentration detected in ground water from the NAWQA study was 0.16 ug/L, 95th percentile concentration values were ND for all wells sampled, and the median value was ND or < 0.002 ug/L. Results from the NAWQA database indicate that diazinon was detected more frequently in shallow ground water in urban areas than in agricultural areas. The results of the NAWQA data for ambient groundwater and surface water are discussed in more detail below.

The relative percentage of samples with detections to total wells sampled from studies in which rural drinking water wells were sampled ranged from 5 to 22.5%. The maximum concentration detected in the rural drinking water wells sampled was 1.0 ug/L, and the 95th percentile concentration values ranged from <0.01 (ND) to <0.3 ug/L depending on the study (see summary data below). Average (mean) concentrations as determined from all samples analyzed were reported to range from 0.012 to <0.3 ug/L. Since most wells were sampled one time only, an average concentration value for diazinon per well is not available.

EFED also used the SCI-GROW model to provide a 90-day average concentration of 0.8 ug/L as an upper bound estimate of diazinon concentrations in shallow ground water. See aforementioned EFED memorandum for details on the model estimate.

Ambient Ground Water Quality

USGS (NAWQA) samples ground water from a variety of sources including newly drilled monitoring wells, production wells (domestic and public-supply wells), springs and tile drains. The USGS generated statistical summaries of the ground water data for all wells sampled, shallow wells sampled, and major aquifer sampled. Data from the shallow wells was characterized as ground water in primarily agricultural areas or in primarily urban areas. The data summarized below in Tables 10-12 were collected from 6/30/92 to 11/15/96. The limit of detection for diazinon was 0.002 ug/L and no metabolites were included in the analyses. No delineation as to which of the wells sampled, if any, were used for drinking water versus other uses was provided.

Table 10. Results for Diazinon (ug/L) from USGS NAWQA monitoring program for all wells sampled[1].

Wells	Samples	Detects *	Range	Mean	95th Percentile	Median
2616	3023	51(1.7%)	0.160-ND	0.014	ND	ND

[1] Range, mean, median and 95th percentile values determined from all samples. Samples below the detection limit (LOD) were given a value of ½ the LOD.

* Percentage detects/number of samples.

The agricultural and urban land-use categories in 11 were represented by wells chosen or designed to sample shallow, recently recharged ground water to determine the effects of specific land uses on water quality.

Table 11. Results for Diazinon (ug/L) from USGS NAWQA monitoring program for shallow wells sampled[1].

Land Use	Wells	Samples	Detects *	Range	Mean	95^{th} Percentile	Median
Urban	301	301	5 (1.7%)	0.010-ND	NR[2]	ND	NR[2]
Agricultural	924	924	5 (0.5%)	0.077	NR	ND	NR

[1] Range, mean, median and 95^{th} percentile values determined from all samples. Samples below the detection limit (LOD) were given a value of ½ the LOD.

[2] Not reported.

* Percentage detects/number of wells.

Sites comprising the "major aquifers" category in Table 12 had no such restrictions on land use or water age, and thus, represent a broader mixture of land uses and ground water depths.

Table 12. Results for Diazinon (ug/L) from USGS NAWQA monitoring program for major aquifers sampled[1].

Wells	Samples	Detects *	Range	Mean	95^{th} Percentile	Median
933	933	17 (1.8%)	0.085-ND	NR[2]	ND	NR[2]

[1] Range, mean, median and 95^{th} percentile values determined from all samples. Samples below the detection limit (LOD) were given a value of ½ the LOD.

[2] Not reported.

* Percentage detects/number of wells.

<u>Drinking Water Wells</u>

As discussed above, data from the USGS NAWQA program reported a 1.82% detection frequency of diazinon in major aquifers, with a maximum concentration of 0.16 μg/L. Major aquifers are defined as those that are major current or future sources of ground water supply within a specific hydrogeologic region. Samples are collected from these aquifers from large drinking water supply wells (production wells). Diazinon results are summarized in Table 12. Among the set of pesticides that NAWQA looked at, diazinon is one of the two insecticides found in these major aquifers (the other is carbaryl). All of the other pesticides found were herbicides (10 of them including atrazine and its degradation product deethylatrazine (DEA), metolachlor, cyanazine, alachlor, bentazon, simazine, prometon, diuron, and tebuthiuron). While there was a low rate of false positives for diazinon in the ground-water program, the number of detects is substantially more than could be accounted for by the false positive rate.

The EPA's National Pesticide Survey (NPS) was designed to determine the frequency of pesticide and nitrate-nitrogen contamination in ground water by sampling community water systems and rural drinking water wells nationwide. A total of 1349 wells were sampled (783 rural domestic wells and 566 community water system wells) were selected based on a random, stratified design and sampled once. Drinking water wells were stratified by location relative to general agricultural use (ranked as high, medium, and low) as opposed to specific compound use and relative vulnerability to ground water contamination. Diazinon was included as an analyte in the survey; however, no diazinon was detected in any sample at a limit of detection of 1.1 ug/L.

Although limited in scope, there were some studies designed to determine the quality of drinking water in an area associated with agricultural uses or designed to sample drinking water (households, community water system and/or rural wells). The results of these studies are outlined below. For details see EFED memorandum previously cited. No metabolites were included in any of the studies' analyses.

A survey of household drinking water supplies from ground-water sources was conducted in Page, Rappahannock and Warren counties in the State of Virginia in 1989 and 1990. Agricultural production in these counties includes fruit trees, cattle, poultry and grains. The area's geology is predominantly shale and limestone with karst topography (limestone outcroppings and sinkholes). One sample from each well was collected by the homeowners as close as possible to the well. The wells selected were considered to be at high risk for contamination based on general water chemistry (high nitrates and chloride concentrations) and proximity to agricultural activities that could contaminate the supply. Wells averaged 200 feet in depth and the limit of detection for the analysis of diazinon was 0.01 ug/L. The results are provided in Table 13.

Table 13. Results from household drinking water study in Virginia for diazinon in ug/L.[1]

County	Wells	Samples	Detects *	Range	Mean	95th Percentile	Median
Page	60	60	6 (10%)	0.103-ND	0.012	0.075	ND

Table 13. Results from household drinking water study in Virginia for diazinon in ug/L.[1]							
County	Wells	Samples	Detects *	Range	Mean	95th Percentile	Median
Rappahannock	40	40	9 (22.5%)	0.262-ND	0.023	0.086	ND
Warren	26	26	0	NA	NA[2]	NA	NA

[1] Range, mean, median and 95th percentile values determined from all samples. Samples below the detection limit (LOD) were given a value of ½ the LOD.

[2] Not applicable.

* Percentage detects/number of wells.

Results from a ground-water monitoring study conducted in eight regions of Missouri to determine the quality of drinking water in agricultural areas are presented below in Table 14. Twenty-five wells in 8 regions (201 wells) were sampled 4 times each (804 samples). Monitoring was conducted quarterly from December 1987 to September 1989 at each well. Five samples were positive for diazinon. Four of the five samples with positive detections were from samples collected in December 1987, and one was from a March 1988 sampling. Diazinon use was documented (354 pounds of active ingredient) in six of the eight regions sampled. Two of these regions had positive detections of diazinon. The limit of detection was 0.3 ug/L.

Table 14. Results from ground-water monitoring study in Missouri for diazinon in ug/L.[1]						
Wells	Samples	Detects *	Range	Mean	95th Percentile	Median
201	804	5 (2%)	1.0-ND	ND	ND	ND

[1] Range, mean, median and 95th percentile values determined from all samples. Samples below the detection limit (LOD) were given a value of ½ the LOD.

* Percentage detects/number of wells.

Results from a study to sample wells from 10 counties in the Mississippi Delta from March 1983 to February 1984 are presented below in Table 15. Wells sampled were 40 to70 feet in depth and selected based on their location in areas with high pesticide usage and agricultural production. The limit of detection was 0.01 ug/L.

Table 15. Results from ground-water monitoring study in Mississippi for diazinon in ug/L.[1]						
Wells	Samples	Detects *	Range	Mean	95th Percentile	Median
143	143	7 (5%)	0.478-ND	0.013	ND	ND

[1] Range, mean, median and 95th percentile values determined from all samples. Samples below the detection limit (LOD) were given a value of ½ the LOD.

* Percentage detects/number of wells.

ii. Surface water (modeling/monitoring)

EFED summarized the results from a variety of surface water monitoring studies that included diazinon as an analyte conducted by the USGS under the NAWQA and Stream Water Quality Network (NASQAN) programs, California state regulatory agencies, and individuals in their memorandum dated 5/11/99 from R. Matzner to C. Eiden. The results of some of these studies are briefly outlined here. In general, diazinon was the most frequently detected insecticide in surface water in the NAWQA program. It is detected more frequently and at higher concentrations in samples from urban sites than at agricultural sites. Surface waters sampled under the program include rivers, streams, and creeks from areas with both agricultural and urban pesticide use. Many of the studies conducted have been located in areas where pesticide use and agricultural production are considered to be high. However, the studies have not been targeted explicitly to diazinon use patterns, *per se*. Based on the data presented in the EFED memorandum, diazinon was detected frequently (35% of NAWQA samples) at concentrations ranging from non-detectable to 3.8 ug/L. The maximum detection reported (3.8 ug/L) was from a stream sampling. The size or relevance of the stream from which the maximum detection was reported to a drinking water source was not given. Degradates of diazinon were not included in the NAWQA analyses.

EFED used the PRZM/EXAMS surface water quality models to provide upper bound estimates on diazinon for comparison to a drinking water level of comparison (DWLOC). Model estimates from a scenario representing diazinon use on peaches using the index resevoir was selected for use in the human health risk assessment as it represented a high-end use pattern. A maximum diazinon concentration of 70 ug/L, and a 90th percentile annual average diazinon concentration of 9.4 ug/L were recommended for use in acute and chronic risk assessments, respectively. The details of the modeling efforts and results are detailed in the EFED memo "Revised Tier 2 EECs for Diazinon" dated 11/14/00.

The upper bound estimates generated with PRZM and EXAMS are intended to be used as screens. When the estimates do not exceed the DWLOC, we can have confidence that there is no unacceptable risk. Conversely, when the DWLOC is exceeded by a model estimate it does not necessarily indicate that there is unacceptable risk as the estimate is likely to be higher than the true concentrations found in the environment.

There are several source of conservatism built into the model estimates. In particular, the site chosen to represent a particular crop is chosen because it is expected to produce concentrations greater than 90% of the sites used for that crop. It is not however a "worst case" site. Secondly, the value represent a concentration that was equaled or exceeded once every 10 years in the model simulation. The use rate used in the simulation was the maximum label rate for that crop. (When the information is useful, and the supporting data is available, typical application rates may also be run.) These estimates were made using the index reservoir.

Ambient Surface Water Quality

The data presented below in Tables 16 through 18 are from USGS' NAWQA program. It appears from these data that concentrations of diazinon in ambient surface water increase with decreasing size of the water body sampled, and that urban areas have a greater frequency of detection and higher concentrations for diazinon than agricultural areas. This is supported by diazinon's use pattern, which is largely urban.

Concentrations in large streams and rivers draining relatively large basins sampled under the NAWQA program (1992 - 1996) ranged from non-detectable to 0.40 ug/L, and the 95th percentile concentration value was 0.07 ug/L. The limit of detection was 0.002 ug/L. Samples were collected during a one year period from the first 20 NAWQA study units (period not given). Samples collected during storm events were excluded to avoid bias resulting from repeated sampling during extreme conditions.

Table 16. Results for Diazinon from USGS NAWQA surface water monitoring program for 14 integrator sites on large streams and rivers (ug/L).						
Sites	Samples	Detects*	Range[1]	Mean	95th Percentile	Median
14	245	111 (45%)	0.4 - ND	NR[2]	0.073	NR

[1] Range and 95th percentile values determined from all samples.

[2] Not reported.

* Percentage of detects/number of samples.

Concentrations in streams in relatively small basins (either agricultural or urban) sampled under the NAWQA program (1992 - 1996) ranged from non-detectable to 1.9 ug/L , and the 95th percentile concentration value was 0.43 ug/L at the urban sites. At the agricultural sites, concentrations ranged from non-detectable to 1.2 ug/L , and the 95th percentile concentration value was 0.027 ug/L The limit of detection was 0.002 ug/L. Samples were collected during a one year period from the first 20 NAWQA study units (period not given). Samples collected during storm events were excluded to avoid bias resulting from repeated sampling during extreme conditions.

Table 17. Results for Diazinon from USGS NAWQA surface water monitoring program for 40 agricultural and 11 urban streams in relatively small basins. (ug/L).							
Land Use	Sites	Samples	Detects*	Range[1]	Mean	95th Percentile	Median
Urban	11	326	244 (75%)	1.9 - ND	NR[2]	0.430	NR
Agricultural	40	1000	169 (17%)	1.2 - ND	NR[2]	0.027	NR

[1] Range and 95th percentile values determined from all samples.

[2] Not reported.

* Percentage of detects/number of samples.

Concentrations in all streams sampled under the NAWQA program (1992 - 1996) ranged from non-detectable to 2.9 ug/L , and the 95th percentile concentration value was 0.24 ug/L at the urban sites. At the agricultural sites, concentrations ranged from non-detectable to 3.8 ug/L , and the 95th percentile concentration value was 0.042 ug/L The limit of detection was 0.002 ug/L.   All samples collected between 4/20/92 and 12/16/96 were included in the calculated statistics.

Table 18. Results for Diazinon from USGS NAWQA surface water monitoring program for all streams sampled (ug/L).							
Land Use	Sites	Samples	Detects*	Range[1]	Mean	95^{th} Percentile	Median
Urban	551	2178	1095 (50%)	2.9 - ND	0.05	0.24	0.003
Agricultural	507	2977	703 (24%)	3.8 - ND	0.017	0.042	ND

[1] Range and 95^{th} percentile values determined from all samples.

[2] Not reported.

[*] Percentage of detects/number of samples.

Sampling along major US rivers (the Rio Grande, Mississippi, Columbia, and Colorado) under the USGS NASQAN program (1995 - 1998) show that 95^{th} percentile concentration values for diazinon ranged from 0.055 to 0.003 ppb. Detection limits were 0.002 ug/L for diazinon. No metabolites were included in the analyses.

Several studies conducted in the San Joaquin Valley along the major rivers there (the San Joaquin, Merced, Russian, Tolumne, Salinas, and Sacramento) by either the USGS, California state agencies, or individuals provide data showing low levels of diazinon in these surface waters. Calculated statistics reported for the 95^{th} percentile concentration of diazinon ranged from non-detectable to 1.7 ppb, and mean concentrations ranged from non-detectable to 1.18 ppb. No metabolites were included in the analyses.

Diazinon has been detected in influent and effluent from Publicly Owned Treatment Works (POTWs) indicating that diazinon is entering sewer systems in urban areas as a result of residential uses. Diazinon has also been detected in air, rain, and fog in California. (See EFED memorandum for details).

<u>Surface-Water Sourced Drinking Water</u>

Pilot Reservoir Monitoring Study

In order to gain additional information on the occurrence of pesticides at vulnerable water supplies, the

Office of Pesticide Programs has initiated a pilot reservoir monitoring study jointly with the NAWQA program of the United States Geological Survey. This study is collecting samples at 12 reservoirs used for drinking water supplies that were chosen to represent a variety of sites that are vulnerable to pesticide contamination from across the United States. Samples were taken at the intake of the drinking water facility and a paired finished water sample was taken at the same time. In addition, some sites had a sample taken at the release from the reservoir when that point was not closely associated with the intake. Samples were taken on at least 12 and up to 22 dates during 1999 and the winter of 2000. Preliminary results (Blomquist, 2000) indicate that diazinon was found in 84 of samples taken at drinking water intakes at concentrations up to 0.11 : g L^{-1}. Diazinon was not found in any of 171 finished water samples. However, the samples were not analyzed for either of the two major diazinon degradates, diazoxon, or oxypyrimidine. There is evidence that diazoxon is formed during drinking water treatment as discussed below. It is worth emphasizing that these are preliminary results and that they have passed through all USGS QA/QC procedures. Additional monitoring is continuing through 2000.

Drinking Water Treatment

The Office of Pesticide Programs has completed a review of the effects of drinking water treatment on pesticides in water (Hetrick *et al.,* 2000). This review indicates that standard drinking water treatment, consisting of flocculation/sedimentation and filtration does not substantially affect concentrations of some pesticides in drinking water. However, this study indicates that disinfection with chlorine, the most common method, converts diazinon to diazoxon, a degradate of toxicological concern. Further, diazoxon is stable to the presence of chlorine in finished water for at least 48 hours (see EFED chapter dated 11/00 for details). Disinfection is performed at greater than 92% of surface water based facilities.

An industry-sponsored study designed to monitor for diazinon and diazoxon in finished drinking water in community water systems sourced by surface water is underway. Once this survey is completed, submitted and reviewed, and if the data are found to be acceptable, HED recommends a reassessment of exposure to diazinon in drinking water.

d. Drinking Water Risk Characterization

EFED provided the following values in Table 19 for use in acute and chronic drinking water risk estimates. The values selected were based on a combination of monitoring and modeling.

Table 19. Estimated diazinon concentrations (ug/L) in drinking water

Type	Acute	Chronic
Surface Water		
Agricultural Use	2.3 - 70	0.19 - 9.4
Urban Use	3.0	0.46
Ground Water	0.002- 0.80	0.002-0.80

It is worth emphasizing that these estimates are based on parent diazinon only. To the extent that toxic degradates are occurring in water resources, the exposure and risk estimates will be greater.

Concentration Estimates for **Acute** Risk Assessment

For surface water, under the acute column, a range of values was provided by EFED. The lower value represents the 95th percentile concentration out of all reported maximum concentrations for diazinon in surface water from all surface water monitoring studies for agricultural (2.3 ug/L) and urban (3.0 ug/L) uses (although potential drinking water sources were included in the overall database for surface water, there was no characterization as to what type of water source the selected values in the table above represent, i.e., large river versus small stream, etc.). The upper value in the range (70 ug/L) represents the annual peak concentration that would be expected to be equaled or exceeded once every ten years at an approximately 90% site for peaches. A ninety percent site is a site that is expected to have concentrations greater the nine out of ten fields that are used to grow that particular crop. For ground water, under the acute column, the value of 0.002 ug/L represents the detection limit from thel ground water monitoring studies. The SCI-GROW estimate of 0.8 ug/L represents a 99th percentile concentration value for pesticides in shallow groundwater (personal communication with Dr. M. Barrett, EFED).

Concentration Estimates for **Chronic** Risk Assessment

For surface water, under the chronic column, a range of values was provided. The lower value represents the 95th percentile of the arithmetic mean concentrations calculated from all reported sample concentrations (detects and non-detects) for diazinon in surface water from all surface water monitoring studies for agricultural (0.19 ug/L) and urban (0.46 ug/L) uses. The upper value (9.4 ug/L) in the range represents the annual mean concentration that would be expected to be equaled or exceeded once every ten years at an approximately 90% site for peaches. A ninety percent site is a site that is expected to have concentrations greater the nine out of ten fields that are used to grow that particular crop. For groundwater, the value of 0.002 ug/L represents the limit of detection from the groundwater monitoring studies and is the same as the value reported for use in acute assessments. Although average values were reported for concentrations of diazinon in groundwater for some studies, the average values were determined from all samples analyzed and not on a per well basis. Average concentration values per well from monitoring data are considered more appropriate for use chronic risk assessment. In the absence of these average values, HED used the 99th percentile model estimate from SCI-GROW and the 95th percentile concentration from monitoring data provided by EFED for comparison against chronic DWLOCs.

Drinking Water Risk from Acute Exposures

HED calculated acute DWLOCs for several other subpopulations of interest. These values are provided in Table 20 below and compared to monitoring data and model estimates of diazinon in surface and groundwater.

In general,

$$DWLOC_{acute}\ (:g/L) = \frac{\text{(acute water exposure, mg/kg/day)(body weight)}}{\text{(water consumption, L/day)}(10^{-3}\ \text{mg/:g})}$$

where acute water exposure = [aPAD (mg/kg/day) - acute food exposure (mg/kg/day)]

The acute PAD is 0.0025 mg/kg/day, and water consumption is 2 L/day for adults and 1 L/day for children; and body weight is 70 kg for total US population and males 13+ years old, 60 kg for females 13+ years old, and 10 kg for children and infants.

Table 20. Comparison of Acute DWLOC Values to Monitoring and Model Concentration Estimates of Diazinon Concentrations in Surface and Ground Waters

Population Group	DWLOC (ppb) for Acute Assessment[1]	Groundwater (ppb)		Surface water (ppb)	
		monitoring	model[2]	monitoring	model
General U.S.	55	0.002	0.80	3	70
All infants (< 1yr)	18	0.002	0.80	3	70
Children (1-6 yrs)	9	0.002	0.8	3	70
Children (7-12 yrs)	17	0.002	0.8	3	70
Females (13-50 yrs)	48	0.002	0.8	3	70
Males (13-19 yrs)	67	0.002	0.8	3	70
Males (20+ yrs)	55	0.002	0.8	3	70
Seniors (55+yrs)	56	0.002	0.8	3	70

[1]The DWLOC acute values were calculated based on dietary exposure including sheep commodities and beef fat.

[2]For ground water, the 90-day average concentration from SCI-GROW represents a 99th percentile concentration in ground water, and is the model concentration estimate used for purposes of comparison against the acute DWLOC values.

Shaded areas = EEC exceeds DWLOC for that subpopulation.

Concentration estimates for acute exposures to diazinon in *groundwater* based on model estimates and monitoring data are less than the acute DWLOC values for all subgroups analyzed. HED concludes there is no acute drinking water concern for diazinon in groundwater-sourced drinking water. Concentration estimates for acute exposures to diazinon in *surface water* based on ambient water quality *monitoring* data are less than the acute DWLOC values for all subgroups analyzed. However, comparing acute DWLOCs values to *model* estimates for concentrations of diazinon in ambient surface water, there is a potential concern for all population subgroups analyzed. Based on the available information, HED cannot conclude that there is no concern for acute exposures to diazinon in surface-water-sourced drinking water. However, it is worth noting that there is substantial uncertainty in the surface water assessment as demonstrated by the difference between the estimates based on monitoring and simulation modeling, and the fact that critical degradates have not been included in the assessment.

Drinking Water Risk from Chronic Exposures

HED calculated chronic DWLOCs for several other subpopulations of interest. These values are provided in 21 below and compared to monitoring data and model estimates of diazinon in surface and groundwater.

In general,

$$DWLOC_{chronic}\ (:g/L) = \frac{\text{(chronic water exposure, mg/kg/day)(body weight)}}{\text{(water consumption, L/day)}(10^{-3}\ \text{mg/:g})}$$

where chronic water exposure* = [cPAD (mg/kg/day) - chronic food exposure (mg/kg/day)]

*[Note: There are no homeowner uses that result in chronic, long-term exposures to diazinon in the home.]

The chronic PAD is 0.0002 mg/kg/day, and water consumption is 2 L/day for adults and 1 L/day for children; and body weight is 70 kg for total US population and males 13+ years old, 60 kg for females 13+ years old, and 10 kg for children and infants .

Table 21. Comparison of Chronic DWLOC Values to Monitoring and Model Concentration Estimates of Diazinon Concentrations in Surface and Ground Waters					
Population Group	DWLOC (ppb) for Chronic Assessment	Groundwater (ppb)		Surface water (ppb)	
		monitoring[2]	model[1]	monitoring	model
General U.S.	6	0.002	0.8	0.5	9
All infants (< 1yr)	2	0.002	0.8	0.5	9
Children (1-6 yrs)	2	0.002	0.8	0.5	9
Children (7-12 yrs)	2	0.002	0.8	0.5	9
Females (13-50 yrs)	6	0.002	0.8	0.5	9
Males (13-19 yrs)	6	0.002	0.8	0.5	9
Males (20+ yrs)	6	0.002	0.8	0.5	9
Seniors (55+yrs)	6	0.002	0.8	0.5	9

[1]For ground water, the 90-day average concentration from SCI-GROW represents the 99th percentile concentration value in groundwater and is compared to the chronic DWLOC values.

Shaded areas = EEC equal to or exceeds DWLOC for that subpopulation

Concentration estimates for long-term, chronic exposures to diazinon in *groundwater* based on monitoring data or modeling estimates are less than the chronic DWLOC values for all subgroups analyzed. HED concludes that there is no concern for chronic exposures to diazinon in groundwater-sourced drinking water. Concentration estimates for chronic exposures to diazinon in ambient *surface water* based on *monitoring* data are less than the chronic DWLOC values for all subgroups. Therefore, there is no concern for chronic exposures to diazinon in surface water-sourced drinking water when concentration estimates are based on monitoring data. However, when comparing chronic DWLOCs values to *model* estimates for concentrations of diazinon in surface water there is a potential concern for all subgroups, in particular infants and children. Therefore, HED cannot conclude that there is no concern for chronic exposures to diazinon in surface-water-sourced drinking water when concentration estimates are based on modeling. However, it is worth noting that there is substantial uncertainty in the surface water assessment as demonstrated by the difference between the estimates based on monitoring and simulation modeling (almost 20x), and the fact that critical degradates have not been included in the assessment.

4. Non-Dietary (Occupational and Residential) Exposure and Risk Characterization

Diazinon is an organophosphate insecticide used extensively in residential settings by both residents and PCOs, and for agricultural use (e.g., citrus, field and vegetable crops, tree fruits, etc.), and outdoor ornamental uses. Registered uses include a wide variety of food, turf and ornamental plants, as well as indoor products, and in pet collars. Diazinon is registered for use in/on sorghum, corn, cotton, citrus, nut crops, cole crops, pome and strawberry fruits, field and vegetable crops, ornamental plants, mushroom houses, sheep, livestock premise treatments, and ear tags. It can also be used in greenhouses, although the registrant has voluntarily agreed to delete this use. It is used in residential and commercial buildings, schools, daycare centers, hotels, restaurants, hospitals, stores, warehouses, food manufacturing plants and vehicles. Targeted pests include fleas, ticks, cockroaches, cutworms, grasshoppers, aphids, etc. There are a wide range of application rates. Typical vegetable crop rates range from foliar application of 0.5 lb ai/acre to soil incorporated rates up to 4 lb ai/acre; granular applications up to 4 lb ai/acre; greenhouse up to 0.08 lb ai/gal; and fruit tree and nut tree (almonds and walnuts) up to 2 and 3 lb ai/acre, respectively. Diazinon is formulated as wettable powders, granulars, impregnated ear tags, microencapsulated, and soluble concentrate/liquids.

Occupational and residential exposures to diazinon can occur during handling, mixing, loading and applying activities. Occupational postapplication exposure can occur for agricultural workers during scouting, irrigation and harvesting activities, and handling seeds. Residential postapplication exposure can occur following treatment of lawns, or residences for cockroaches, ants, and other insects. In addition, there is a potential for inadvertent oral exposure to children from putting fingers or objects in their mouths (hand to mouth activities) following contact with treated surfaces or turf, or incidentally ingesting diazinon-treated turf or soil. Postapplication exposure to children can occur in locations other than the home, including schools, daycare centers, playgrounds, and parks. Based on toxicological criteria and potential for exposure, HED has conducted dermal and inhalation exposure assessments for the occupational and residential handlers, occupational postapplication, in addition to residential postapplication dermal, inhalation to adults and children and inadvertent oral exposure to children.

In July 2000, the registrants agreed to discontinue to support the registration of indoor uses. This includes use inside any structure or vehicle, vessel, or aircraft and/or on any contents therein.

Details of the occupational and residential exposure scenarios are presented in the attached memorandum from D. Smegal/T. Leighton to B. Chambliss and D. Drew (D270837, 11/30/00).

a. Occupational Handler Exposure

(i) Occupational Handler Exposure Scenarios

HED has identified 32 major exposure scenarios (resulting in 76 assessments based on range of application rates) for which there is potential occupational handler exposure during mixing, loading, and applying products containing diazinon to agricultural crops and ornamentals and to non-agricultural use sites such as residential or recreational settings. These occupational scenarios reflect a broad range of application equipment, application methods and use sites. For agricultural uses, application techniques include tractor-drawn equipment, open and closed mixing/loading, and hand held equipment. The application rates used in the assessment are intended to reflect the upper range of rates on the labels. Maximum rates are always included in the assessment to provide a hazard evaluation for those individuals that may use the label as approved by the Agency.

The scenarios were classified as short-term (1 to 7 days), intermediate-term (1 week to 6 months) and in some cases long-term (greater than 6 months) based primarily on frequency of exposure. The occupational handler scenarios are expected to be of a short-, intermediate and long-term durations. For the agricultural handlers, the estimated exposures considered baseline (long pants, long sleeved shirt, no gloves), personal protective equipment (PPE, which includes a double layer of clothing and gloves and/or a dust/mist respirator), and engineering controls (closed mixing/loading systems for liquids and granulars and enclosed cabs/trucks). The list of scenarios assessed are as follows:

(1) Mixing/loading liquids to support:

- (a) aerial applications;
- (b.) chemigation applications;
- u. groundboom applications;
- (d) airblast applications;
- (e) support rights-of-way-sprayer applications; and
- (f) high-pressure hand-wand (livestock areas, greenhouses) applications*.

(2) Mixing/loading wettable powders to support:

- C aerial applications;
- C chemigation applications;
- C groundboom applications;
- (d) airblast applications;
- (e) rights-of-way-sprayer applications;
- (f) high-pressure handwand (livestock areas, greenhouses) applications*, and
- C Seed treatment.

(3) Loading granules to support tractor-drawn broadcast spreaders applications.

(4) Applying sprays or liquids with:

- (a) an airblast;
- (b) a groundboom.;
- (c) a paintbrush*;
- (d) an airless sprayer;
- (e) a high-pressure handwand (livestock areas, greenhouses)*;
- (f) a rights-of-way sprayer; and
- (g) a fixed-wing aircraft.

(4) Applying granules with a tractor drawn spreader.

(6) Flagging for sprays.

(7) Mixing/loading/applying liquids with:

   (a) a low pressure hand-wand (pest control operators, PCOs)*;

   (b) a backpack sprayer*;

   (c) a high pressure hand-wand (livestock areas, greenhouse)*, and

   (d) a handgun sprayer used by a lawn care operator (LCO) (lawn)*.

(8) Mixing/loading/applying wettable powders with

   (a) a low pressure hand-wand (PCOs)*, and

   (b) a handgun sprayer used by a LCO (lawn)*.

(9) Loading/applying granules with:

   (a) a belly grinder; and

   (b) a push-type spreader*.

(10) Applying diazinon dust formulations by a PCO.

Use scenarios noted with an asterisk (*) have the potential for long-term exposures. Potential risks from any long-term exposures that may occur under these use scenarios are adequately addressed by the intermediate-term exposure assessment because both risk assessments use the same dermal and inhalation toxicological endpoint.

As noted previously, in July 2000, Novartis stated that they do not plan to support the belly grinder and airless sprayer methods of application, or any indoor use. However, HED included the belly grinder and airless sprayer analyses for completeness, since the labels have yet to be modified to reflect this change.

(ii) Occupational Handler Exposure Data Sources and Assumptions

Only one chemical specific applicator study was submitted by the registrant, which is the application of a 2% diazinon dust formulation by a pest control operator (PCO) indoors (Hayes et al. 1980, as summarized in MRID 44348801). In this study, Novartis estimated the PCO absorbed dose of 2.2 µg/kg/day based on the urine biological monitoring for 14 individuals over 3 months. The total amount of diazinon applied was not reported. The peak air concentrations were 41 µg/m^3, with a geometric mean air concentration of 3.8 µg/m^3. The inhalation exposure was estimated to be 0.76 µg/kg/day based on the following assumptions and equation: 1.7 m^3/hr*8 hr/day*3.8 µg/m^3 / 70 kg. This study was used to assess exposures and risks to PCOs during dust application.

No other chemical-specific occupational mixer/loader/applicator data were available for supporting the reregistration of diazinon. Therefore, recent Occupational and Residential Exposure Task Force (ORETF) data, along with surrogate data from PHED V1.1 were used to assess the potential handler exposures to diazinon. Recent ORETF data (MRID 44972201, based on Dacthal) for a handgun lawn sprayer (scenarios 7b and 8b), and push-type spreader (scenario 9b) were utilized in this assessment. In addition, seed treatment data from a lindane seed treatment study (dust formulation, MRID 44405802) were used for a screening-level assessment of the diazinon seed treatment scenario.

In the absence of applicable chemical-specific and ORETF data, agricultural handler and LCO/PCO potential exposures resulting from handling and applying diazinon were estimated using data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 or the Draft Residential SOPs. PHED was designed by a Task Force of representatives from the U.S. EPA, Health Canada, the California Department of Pesticide Regulation, and member companies of the American Crop Protection Association. PHED is a software system consisting of two parts -- a database of measured exposure values for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates). HED's policy is to supplement chemical-specific data with available surrogate data in PHED to increase the sample size (U.S. EPA and HC 1995a - PHED V1.1 Evaluation Guidance). This policy is in effect because individual chemical-specific studies, even when fulfilling the Guideline minimum number of replicates, do not necessarily encompass the variety of equipment in use throughout the country and the large variability of exposures among handlers. While data from PHED provides the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handled) may not accurately represent labeled uses in all cases.

Potential exposures were calculated using unit exposures (i.e., normalized to amount of active ingredient handled -- mg/lb ai handled) from passive dosimetry data extrapolated to be representative of the maximum rates on the label (in some instances to typical rates). The normalized exposure data are extrapolated by multiplying by the amount of diazinon handled per day (i.e., lb ai/day). The amount of diazinon assumed handled per day was derived from the various application rates and the number of acres (or gallons of spray solution) that could be applied in a single day.

The potential exposures within the 32 identified exposure scenarios are assessed in this RED chapter using the toxicological endpoints and uncertainty factors associated with the active ingredient. Therefore, the PPE and engineering controls are determined by the assessment of the active ingredient and not the currently required PPE/engineering control measures on diazinon labels. This distinction of determining risk mitigation measures based on the active ingredient instead of the label required PPE is important because of the nature of the end-use products. The toxicological endpoint and associated uncertainty factors are often more sensitive than the end-use product's toxicity categories that were used to set the existing label PPE. On the other hand, some end-use products require additional PPE that are not necessary for the active ingredient because of the end-use product's potential for eye and/or skin irritation based on inerts.

(iii) Occupational Handler Risk Characterization

A summary of the short-, intermediate- and long-term risk estimates for baseline, PPE and engineering controls is presented in **Table 22** for occupational handlers. As noted previously, this assessment includes both agricultural workers and LCOs/PCOs at non-agricultural use sites, such as residential and recreational settings. **Table 22** also provides a summary of the range of application rates assessed for diazinon.

MOEs for occupational handlers were derived by dividing the appropriate NOAEL or LOAEL, shown on **Table 2**, by the daily dermal or inhalation exposure estimate. As noted previously, a NOAEL of 1 mg/kg/day from a dermal toxicity study was used to assess dermal exposures (all durations), while a lowest-observed-adverse-effect level (LOAEL) of 0.026 mg/kg/day from an inhalation toxicity study was selected to assess inhalation exposures (all durations). Because route-specific toxicity studies are available, dermal and inhalation absorption factors are not necessary. Cholinesterase inhibition (plasma, red blood cell and/or brain) is the critical effect for all routes of exposure. Oral exposures were not evaluated for workers or adult residents.

For the dermal and inhalation risk assessments, risk estimates are expressed in terms of the Margin of Exposure (MOE), which is the ratio of the NOAEL or LOAEL selected for the risk assessment to the exposure. Target margins of exposure (MOEs) for short-term dermal risk assessments are 100 resulting from the following uncertainty factors: a 10x for inter-species variability and 10x for intra-species extrapolation. A target MOE of 300 is applicable for the intermediate- and long-term dermal endpoints based on the inter- (10X) and intra-species factors (10X), in addition to a 3X to extrapolate from a 21-day dermal study to longer-term exposures. For inhalation risk assessments (all time periods) the target MOE is 300 resulting from the inter- (10x) and intra-species (10X) factors, and for lack of a NOAEL in the critical study and consequent use of a LOAEL (3x). MOEs below the target level would represent a risk concern.

Dermal and inhalation exposures were combined because of a common toxicity endpoint (i.e., cholinesterase inhibition), and because dermal and inhalation exposures may occur simultaneously. An aggregate risk index (ARI) was used to combine short-term dermal and inhalation risk estimates because the dermal and inhalation target MOEs are different (i.e., 100 for dermal and 300 for inhalation). An ARI of less than one exceeds HED's level of concern. However, a total MOE was calculated for intermediate- and long-term exposures because the target MOE is 300 for both dermal and inhalation exposure. For intermediate- and long-term aggregate exposure, an MOE of less than 300 exceeds HED's level of concern.

The results of the occupational handler assessments are shown on **Table 22.** The majority of occupational risk estimates for handlers exposed to diazinon exceed HED's level of concern, even with PPE and/or engineering controls. HED identified 32 major handler scenarios, which when combined with the typical range of application rates resulted in 76 scenarios. The results of the agricultural handler assessments indicate that <u>none</u> of the potential exposure scenarios provide ARIs ≥1 for short-term durations or total dermal and inhalation MOEs greater than or equal to 100 and 300, respectively for intermediate and long-term durations at baseline attire (i.e., long pants, long sleeved shirts, no gloves). Only 5 of the short-term scenarios quantitatively evaluated using personal protective equipment (PPE) (long sleeved shirt, long pants, shoes, socks, chemical-resistant gloves, and dust/mist respirator) or by using engineering controls (e.g., closed mixing systems or enclose cabs) have a ARIs ≥1, while only 4 scenarios have total dermal and inhalation MOEs ≥300. There are insufficient data to adequately assess the sheep treatments, exterior paint additive uses and mushroom houses, and additional data are requested to support these uses. The agricultural handler assessments are believed to be reasonable representations of diazinon uses. Surrogate Pesticide PHED data were used to assess handler exposure because no chemical specific studies are available, except for one study that evaluated application of dust formulation by a pest control operator (PCO) (MRID 44348801).

For specific details and calculations of inhalation, dermal, and total exposures, ARIs and MOEs see the attached memorandum from D.Smegal/T. Leighton to B. Chambliss and D. Drew, D270837**,** November 30 2000.

Uncertainties: The handler assessments are believed to be reasonable high end representations of diazinon uses. There are, however, many uncertainties in these assessments. The assessment provides the estimated exposures for the maximum labeled rates stipulated on the labels, and other rates such as the lower rates for foliar applications to assist the regulatory risk managers in their decisions. HED believes this assessment is realistic and yet provides a reasonable certainty that the exposures are not underestimated. The assumptions and uncertainties identified below are included for characterization and transparency:

C *Application Rates:* Each exposure scenario includes the label maximum application rate. In addition, a range of application rates was used when the maximum application rates for various crops varied widely. Other than a national survey, there are no statistical techniques to determine what rates to include in an assessment -- other than always including the maximum rates. In most instances, the maximum labeled application rates were used with application techniques that are feasible, given the amount of dilute spray that needs to be applied.

C *Amount Handled:* The daily acres treated are HED standard values along with the amount of gallons that may be applied using handheld equipment. In this deterministic approach, central tendency values for unit exposures from PHED are mixed with high end input parameters such as the application rate and acres treated.

C *Unit Exposures:* The unit exposure values calculated by PHED generally range from the geometric mean to the median of the selected data set. To add consistency and quality control to the values produced from this system, the PHED Task Force has evaluated all data within the system and has developed a set of grading criteria to characterize the quality of the original study data. The assessment of data quality is based on the number of observations and the available quality control data. These evaluation criteria and the caveats specific to each exposure scenario are summarized in the PHED Surrogate Exposure Guide dated August 1998. While data from PHED provides the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handled) may not accurately represent labeled uses in all cases.

C *Exposure Factors:* The ratio of the body surface area used in dermal calculations to the body weight to estimate potential dose overestimates by a factor of 1.1. The ratio is not physiologically matched in that the surface area is for an average male while the body weight is the median for both male/female. The reduction factor would increase a dermal MOE from 8 to 9 or 90 to 100.

HED has agreed to use the NAFTA recommended values for breathing rate rather than the existing rate in Series 875 Group A (i.e., previously known as Subdivision U). Series 875 Group A recommends an inhalation rate of 29 L/min. The new NAFTA recommended inhalation rates are 8.3, 16.7, and 26.7 L/min for sedentary activities (e.g., driving a tractor), light activities (e.g., flaggers and mixer/loaders < 50 lb containers), and moderate activities (e.g., loading > 50 lb containers, handheld equipment in hilly conditions), respectively. These inhalation reduction factors are 3.5 for tractor drivers, 1.7 for mixer/loaders and flaggers, and 1.1 for handheld equipment. These changes in exposure factors will be programmed in PHED V2.0 and are characterized in this document for regulatory risk management decisions.

These uncertainties are inherent in most pesticide exposure assessments. The conservative nature of the assessments, however, are believed to be protective of the handlers.

Table 22

Exposure Variables and Risk Estimates for

Agricultural and Commercial Handler Uses of Diazinon

Short-, Intermediate- and Long-Term (as applicable) Durations

Exposure Scenario (Scenario#) (g)	Application Rates (lb ai/acre) (unless noted) (a)	Daily Acres Treated (b)	Baseline MOEs (c,d)		PPE MOEs (c,e)				Engineering Controls MOEs (c,f)			
			Dermal	Inhalation	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300
Mixer/Loader Exposure												
Scenario #1 -Mixing/Loading Liquids												
Aerial Application (1a)	0.5 (foliar cole crops)	350	0.14	8.7	24	87	0.13	19	47	130	0.22	34
	1.25 foliar corn	350	0.06	3.5	9.4	35	0.05	7.4	19	50	0.09	14
		1200	0.016	1	2.7	10	0.02	2.2	5.4	15	0.03	4
Chemigation (1b)	3 (max) (cranberries)	35	0.23	15	39	150	0.21	31	77	210	0.37	56
Groundboom Application (1c)	0.75 foliar	80	0.4	25	69	250	0.38	54	**140**	**370**	0.64	100
		200	0.16	10	28	100	0.15	22	54	150	0.26	40
	4 (preplant, max)	80	0.075	4.7	13	47	0.07	10	25	69	0.12	19
		200	0.03	1.9	5.1	19	0.03	4	10	27	0.05	7.4

Table 22

Exposure Variables and Risk Estimates for

Agricultural and Commercial Handler Uses of Diazinon

Short-, Intermediate- and Long-Term (as applicable) Durations

Exposure Scenario (Scenario#) (g)	**Application Rates (lb ai/acre) (unless noted) (a)**	**Daily Acres Treated (b)**	**Baseline MOEs (c,d)**		**PPE MOEs (c,e)**				**Engineering Controls MOEs (c,f)**			
			Dermal	**Inhalation**	**Dermal**	**Inhalation**	**Total ARI (short-term) Target ARI 1**	**Total MOE (Intermediate and Long Term) Target MOE 300**	**Dermal**	**Inhalation**	**Total ARI (short-term) Target ARI 1**	**Total MOE (Intermediate and Long Term) Target MOE 300**
Airblast Application (1d)	1 (hops/grapes) (k)	20	1.2	76	**200**	**760**	**1.13**	160	**400**	**1100**	**1.93**	**300**
		40	0.6	38	**100**	**380**	0.57	81	**200**	**550**	0.96	150
	2 (fruit trees) (k)	20	0.6	38	**100**	**380**	0.57	81	**200**	**550**	0.96	150
		40	0.3	19	52	190	0.28	40	**100**	**270**	0.48	74
	3 (nut trees) (j,k)	20	0.4	25	69	250	0.38	54	**140**	**370**	0.64	100
Rights-of-Way Sprayer (1e)	0.5	40	1.2	76	**210**	**760**	**1.13**	160	**400**	**1100**	**1.9**	**300**
High-pressure Handwand (Livestock Areas, greenhouses) (1f) *	0.04lb ai/gal (h)	1000 gal/day	0.6	38	**100**	**380**	0.57	81	**200**	**550**	0.96	150
	0.08 lb ai/gal (h)		0.3	19	52	190	0.28	40	**100**	270	0.48	74
Scenario #2 -Mixing/Loading Wettable Powders												

Table 22

Exposure Variables and Risk Estimates for

Agricultural and Commercial Handler Uses of Diazinon

Short-, Intermediate- and Long-Term (as applicable) Durations

Exposure Scenario (Scenario#) (g)	Application Rates (lb ai/acre) (unless noted) (a)	Daily Acres Treated (b)	Baseline MOEs (c,d)		PPE MOEs (c,e)				Engineering Controls MOEs (c,f)			
			Dermal	Inhalation	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300
Aerial Application (2a)	0.5 (foliar cole crops)	350	0.11	0.24	3.1	2.4	0.01	1.3	19	43	0.08	13
	1.25 foliar corn	350	0.043	0.1	1.2	0.97	0.003	0.5	7.6	17	0.03	5.3
		1200	0.013	0.03	0.36	0.28	0.001	0.16	2.2	5.1	0.01	1.5
Chemigation (2b)	3 (cranberries)	35	0.19	0.4	5.2	4	0.01	2.3	32	72	0.13	23
Groundboom Application (2c)	0.75 foliar	80	0.32	0.71	9	7	0.019	4	56	130	0.24	39
		200	0.13	0.28	3.6	2.8	0.007	1.6	22	51	0.1	15
	4 (preplant, max)	80	0.06	0.13	1.7	1.3	0.003	0.74	10	24	0.04	7
		200	0.024	0.05	0.68	0.53	0.001	0.3	4.2	9.5	0.02	3
Airblast Application (2d)	1 (hops/grapes) (k)	20	0.94	2.2	26	21	0.06	12	**170**	**380**	0.72	120
		40	0.47	1.1	13	11	0.03	6	83	190	0.36	60
	2 (fruit trees) (k)	20	0.48	1.1	13	11	0.03	6	83	190	0.36	60
		40	0.24	0.53	6.7	5.3	0.01	3	42	95	0.18	29
	3 (nut trees) (j,k)	20	0.32	0.71	9	7	0.02	4	56	130	0.24	39

Table 22

Exposure Variables and Risk Estimates for

Agricultural and Commercial Handler Uses of Diazinon

Short-, Intermediate- and Long-Term (as applicable) Durations

Exposure Scenario (Scenario#) (g)	**Application Rates (lb ai/acre) (unless noted) (a)**	**Daily Acres Treated (b)**	**Baseline MOEs (c,d)**		**PPE MOEs (c,e)**				**Engineering Controls MOEs (c,f)**			
			Dermal	**Inhalation**	**Dermal**	**Inhalation**	**Total ARI (short-term) Target ARI 1**	**Total MOE (Intermediate and Long Term) Target MOE 300**	**Dermal**	**Inhalation**	**Total ARI (short-term) Target ARI 1**	**Total MOE (Intermediate and Long Term) Target MOE 300**
Rights-of-Way Sprayer (2e)	0.5	40	0.95	2.1	27	21	0.06	12	**170**	**380**	0.72	120
High-pressure Handwand (Livestock Areas, greenhouses) (2f) *	0.04lb ai/gal (h)	1000 gal/day	0.47	1.1	13	11	0.03	5.9	83	190	0.36	58
	0.08 lb ai/gal (h)		0.24	0.53	6.7	5.3	0.01	3	42	95	0.18	29
Seed Treatment (2g) (l)	0.094 lb ai/bushel	50 bushels (corn)	ND	240	1.6	**2400**	0.02	1.6	**Not Feasible**			
Applicator Exposure												
Scenario #3 - Loading Granules												
Tractor-drawn broadcast spreaders (3)	4 (preplant, max)	80	26	3.4	64	34	0.1	22	**1300**	170	0.53	150
		200	10	1.	26	13	0.04	8.8	**510**	67	0.21	60
Scenario #4 -Applying sprays/liquids												

Table 22

Exposure Variables and Risk Estimates for

Agricultural and Commercial Handler Uses of Diazinon

Short-, Intermediate- and Long-Term (as applicable) Durations

Exposure Scenario (Scenario#) (g)	**Application Rates (lb ai/acre) (unless noted) (a)**	**Daily Acres Treated (b)**	**Baseline MOEs (c,d)**		**PPE MOEs (c,e)**				**Engineering Controls MOEs (c,f)**			
			Dermal	**Inhalation**	**Dermal**	**Inhalation**	**Total ARI (short-term) Target ARI 1**	**Total MOE (Intermediate and Long Term) Target MOE 300**	**Dermal**	**Inhalation**	**Total ARI (short-term) Target ARI 1**	**Total MOE (Intermediate and Long Term) Target MOE 300**
Airblast (4a)	1 (hops/grapes) (k)	20	9.8	20	16	200	0.13	15	**180**	200	0.49	96
		40	4.9	10	8	100	0.06	7.4	92	100	0.25	48
	2 (fruit trees) (k)	20	5	10	8	100	0.06	7.4	92	100	0.25	48
		40	2.4	5	4	50	0.03	3.7	46	51	0.12	24
	3 (nut trees) (j,k)	20	3.2	6.7	5.3	67	0.04	4.9	61	67	0.16	32
Groundboom Tractor (4b)	0.75 foliar	80	83	41	**120**	**410**	0.63	91	**230**	**700**	**1.2**	180
		200	33	16	47	160	0.25	36	93	280	0.47	70
	4 (preplant, max)	80	16	7.7	22	77	0.12	17	44	130	0.22	33
		200	6.3	3.1	8.8	31	0.05	7	18	53	0.09	13
Paintbrush (4c) (fly control)	0.04 lb ai/gal (i)	5 gal/day	1.9	33	16	**330**	0.14	15	Not Feasible			
	0.08 lb ai/gal (i)		0.97	16	8	160	0.07	7.6				

Table 22

Exposure Variables and Risk Estimates for

Agricultural and Commercial Handler Uses of Diazinon

Short-, Intermediate- and Long-Term (as applicable) Durations

Exposure Scenario (Scenario#) (g)	Application Rates (lb ai/acre) (unless noted) (a)	Daily Acres Treated (b)	Baseline MOEs (c,d)		PPE MOEs (c,e)				Engineering Controls MOEs (c,f)			
			Dermal	Inhalation	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300
Airless Sprayer (4d) (fly control)	0.04 lb ai/gal (i)	40 gal/day	1.2	1.4	3.1	14	0.02	2.5	Not Feasible			
	0.08 lb ai/gal (i)		0.58	0.69	1.6	6.9	0.01	1.3				
High-pressure Handwand (Livestock Areas, greenhouses) (4e)*	0.04lb ai/gal (h)	1000 gal/day	0.97	0.58	4.9	5.8	0.01	2.6	Not Feasible			
	0.08 lb ai/gal (h)		0.49	0.29	2.5	2.9	0.01	1.3				
Rights-of-Way Sprayer (4f)	0.5	40	2.7	23	12	230	0.1	11	Not Feasible			
Fixed-wing Aircraft –Enclosed Cockpit (4g)	0.5 (foliar cole crops)	350	No Open cockpit data available						80	150	0.31	53
	1.25 foliar corn	350							32	61	0.12	21
		1200							9	18	0.04	6.1

Table 22

Exposure Variables and Risk Estimates for

Agricultural and Commercial Handler Uses of Diazinon

Short-, Intermediate- and Long-Term (as applicable) Durations

Exposure Scenario (Scenario#) (g)	Application Rates (lb ai/acre) (unless noted) (a)	Daily Acres Treated (b)	Baseline MOEs (c,d)		PPE MOEs (c,e)				Engineering Controls MOEs (c,f)			
			Dermal	Inhalation	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300
Scenario #5 -Applying granules												
Tractor-Drawn Granular Spreader (5)	4 (preplant, max)	80	22	4.7	52	47	0.12	25	**100**	26	0.08	21
		200	8.8	1.9	21	19	0.05	9.9	42	10	0.03	8

Table 22
Exposure Variables and Risk Estimates for
Agricultural and Commercial Handler Uses of Diazinon
Short-, Intermediate- and Long-Term (as applicable) Durations

Exposure Scenario (Scenario#) (g)	Application Rates (lb ai/acre) (unless noted) (a)	Daily Acres Treated (b)	Baseline MOEs (c,d)		PPE MOEs (c,e)				Engineering Controls MOEs (c,f)			
			Dermal	**Inhalation**	**Dermal**	**Inhalation**	**Total ARI (short-term) Target ARI 1**	**Total MOE (Intermediate and Long Term) Target MOE 300**	**Dermal**	**Inhalation**	**Total ARI (short-term) Target ARI 1**	**Total MOE (Intermediate and Long Term) Target MOE 300**
Flagger Exposure												
Scenario #6 -Flagging												
Spray Applications (6)	0.5 (foliar cole crops)	350	36	30	40	**300**	0.28	35	**1800**	**1500**	**3.9**	**820**
	1.25 foliar corn	350	15	12	16	120	0.11	14	**730**	**590**	**1.6**	**330**
		1200	4.2	3.5	4.7	35	0.03	4	**210**	170	0.45	95
Mixer/Loader/Applicator Exposure												
Scenario #7 -Mixing/loading/applying liquids												
Low Pressure Handwand (Pest Control Operators, PCOs, livestock areas) (7a) *	0.04 lb ai/gal (h)	40 gal	0.44	38	**120**	**380**	0.61	90	Not Feasible			
	0.08 lb ai/gal (h)		0.22	19	59	190	0.31	45				

Table 22

Exposure Variables and Risk Estimates for

Agricultural and Commercial Handler Uses of Diazinon

Short-, Intermediate- and Long-Term (as applicable) Durations

Exposure Scenario (Scenario#) (g)	Application Rates (lb ai/acre) (unless noted) (a)	Daily Acres Treated (b)	Baseline MOEs (c,d)		PPE MOEs (c,e)				Engineering Controls MOEs (c,f)			
			Dermal	Inhalation	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300
Backpack Sprayer (livestock, PCOs) (7b) *	0.04 lb ai/gal	40 gal	ND	38	27	**380**	0.22	26	Not Feasible			
High Pressure Handwand (livestock areas, greenhouse uses) (7c) *	0.04 lb ai/gal (typical) (h)	1000 gal/day	0.5	0.38	1.1	3.8	0.01	0.85	Not Feasible			
	0.08 lb ai/gal (h)		0.25	0.19	0.5	1.9	0.003	0.42				
Handgun Sprayer (Lawn Care Operator, LCO) (7d)*	4	3	8.3	100	23	**1000**	0.22	23	Not Feasible			
		5	5	61	14	**610**	0.13	14				
Scenario #8 -Mixing/loading/applying Wettable Powders												
Low Pressure Handwand (8a) (PCOs)*	0.04 lb ai/gal (min)	40 gal	5.1	1	7.1	10.3	0.02	4.2	Not Feasible			

Table 22

Exposure Variables and Risk Estimates for

Agricultural and Commercial Handler Uses of Diazinon

Short-, Intermediate- and Long-Term (as applicable) Durations

Exposure Scenario (Scenario#) (g)	Application Rates (lb ai/acre) (unless noted) (a)	Daily Acres Treated (b)	Baseline MOEs (c,d)		PPE MOEs (c,e)				Engineering Controls MOEs (c,f)			
			Dermal	Inhalation	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300
Handgun Sprayer (Lawn Care Operators) (8b)*	4.1	3	5.8	2.5	15	25	0.05	9.5	Not Feasible			
		5	3.5	1.5	9.2	15	0.03	5.7				

Table 22

Exposure Variables and Risk Estimates for

Agricultural and Commercial Handler Uses of Diazinon

Short-, Intermediate- and Long-Term (as applicable) Durations

Exposure Scenario (Scenario#) (g)	Application Rates (lb ai/acre) (unless noted) (a)	Daily Acres Treated (b)	Baseline MOEs (c,d)		PPE MOEs (c,e)				Engineering Controls MOEs (c,f)			
			Dermal	Inhalation	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300	Dermal	Inhalation	Total ARI (short-term) Target ARI 1	Total MOE (Intermediate and Long Term) Target MOE 300
Scenario #9 - Loading/applying Granules												
Belly Grinder (9a)	3.7 (typical) (i)	1	1.9	8	3.3	80	0.03	3.2	Not feasible			
	4.4 (max)		1.6	6.7	2.8	67	0.02	2.7				
Push-type spreader (9b) (LCOs)*	3.7 (typical) (i)	3	20	24	25	230	0.2	24	Not Feasible			
	4.4 (max)		17	20	22	200	0.16	20				
	3.7 (typical) (i)	5	12	14	16	140	0.12	14				
	4.4 (max)		10	12	13	120	0.1	12				
Scenario #10 - Applying Dust Formulation												
Dust Application (PCO) (MRID 44348801)	2% formulation	total amount unknown	not estimated	35	No Data				Not Feasible			

(a) Application rates are a range of representative and maximum rates values found in the diazinon labels. The following labels were used to determine the rates: (1) Wettable powders - EPA Reg. No. 100-460 (Diazinon 50 W) for crops and right-of-way (i.e., 0.5 lb ai/A). Max. rate represents beans, beets, broccoli, etc.

(2) Liquid formulations - EPA Reg. Nos. 100-784 (AG600 WBC) and 100-461 (AG500 emulsifiable solution). Max. rate represents beans, etc. Rights-of-way rate is located on the EPA Reg. No. 100-461. EPA Reg No. 9779-210 states maximum right of way application rate is 0.5 lb ai/A for grasshoppers. Typical right of way application of rate of 1 lb ai/A is based on BEAD estimates (QUA memo from A. Halvorson 1/29/1999).

(3) Granular - EPA Reg. No. 100-469 (Diazinon 14G) and Diazinon Granular Lawn Insect Control (2 percent).

(b) Daily acres treated are are based on HED's estimates of acreage (or gallonage) that would be reasonably expected to be treated in a single day for each exposure scenar concern.

(c) Margin Of Exposure (MOE) = Inhalation (for all time frequencies) LOAEL (0.026 mg/kg/day)/Daily Inhalation Dose or Dermal NOAEL of 1 mg/kg/day/daily dermal exposure (non-absorbed). Where Daily Dermal Dose (mg/kg/day) = [Unit exposure (mg/lb ai) * Application Rate (lb ai/A or per gallon) * Acres or gallons treated] / 70 kg BW, and Daily inhalation Dose (mg/kg/day)= Unit exposure [(g/lb ai) * (1mg/1000 g) Conversion * Application Rate (lb ai/A or per gallon) * Acres or gallons treated]/70 kg BW}. **The target MOE is 100 for short-term dermal exposure, and is 300 for intermediate- and long-term dermal exposure, and 300 for all inhalation exposures.**

(d) Baseline dermal unit exposure represents long pants, long sleeved shirt, no gloves, open mixing/loading, and open cab tractor. Baseline data are not available for aerial application or backpack dermal assessment.

(e) Additional Personal Protective Equipment (PPE) to reduce dermal exposures = workers wearing coveralls over single layer clothing and chemical resistant gloves [Doubl Layer Clothing with Chemical Resistant Gloves (DLC, CRG)]. PPE data are not available for aerial application. A ½ mask for inhalation exposure was assumed to provide a 90% protection factor.

(f) Engineering Controls = single layer clothing and no gloves (except where noted chemical resistant gloves -- because the no glove scenario is not available) and closed m systems and enclosed cab tractors.

(g) The following scenarios, designated with a '*' have the potential for long-term exposure (1f, 2f, 4e, 7a, 7b, 7c,7d, 8a, 8b and 9b).

(h) The 0.08 lb ai/gal is used for longer residual. Both the 0.04 and 0.08 lb ai/gal are for indoor livestock areas, and it was assumed that these rates are applicable to outdoor livestock areas. Paintbrush and airless sprayer are used for fly control in livestock areas.

(i) Typical, average application rate of 3.7 lb ai/A is based on BEAD estimates (QUA memo from A. Halvorson 1/29/1999).

(j) Walnut foliar spray from EPA Reg 100-460 for wettable powder and EPA Reg. 100-461 for liquids (Ag 500).

(k) Acreage treated of 40 acres is applicable to the concentrate (20 gal/A) as per EPA Reg 100-460 instructions. 20 acres is for up to 400 gallons of dilute spray/A (400-461 liquid Ag 500).

(l) Based on a lindane seed treatment study (MRID 44405802) based on a dust formulation.

b. Occupational Postapplication Exposure

(i) Occupational Postapplication Exposure Scenarios

EPA has determined that there is potential exposure to persons entering treated sites (e.g., harvesters) after application is complete. Postapplication exposure data were required during the diazinon DCI of the reregistration process, since, at that time, one or more toxicological criteria had been triggered. Two postapplication studies (i.e., residue dissipation) have been submitted along with the registrant's participation in the Agricultural Reentry Task Force (ARTF). The two crop-specific residue study data are used in HED's risk assessment as surrogates to represent other crops not monitored but currently registered. Activity-specific transfer coefficients, developed by the ARTF, are also used to assess postapplication exposures and risks.

This assessment incorporates the revised policy for agricultural transfer coefficients (i.e., HED Exposure SAC Policy 3.1: *Agricultural Transfer Coefficients* dated August 7, 2000). The revised transfer coefficient policy entailed linking worker activities to more specific crop groupings and using the newly available occupational postapplication exposure data from the ARTF. In the new policy, transfer coefficients were selected to represent the activities associated with 18 distinct crop/agronomic groupings based on different types of vegetables, trees, berries, vine/trellis crops, turf, field crops, and bunch/bundle crops. Diazinon uses were identified in 13 of the 18 groupings. The following 13 crop groupings are used to assess the postapplication exposures to diazinon:

(1) Low berry;
(2) Bunch/Bundle;
(3) Field row crop, low & medium;
(4) Field row crop, tall;
(5) Field-grown nursery ornamentals;

(6) Deciduous tree fruit;

(7) Nut Trees;

(8) Root vegetables;

(9) Cucurbit vegetables;

(10) Fruiting vegetables;

(11) Brassica vegetables;

(12) Leafy vegetables; and

(13) Vine & trellis crops.

The revised policy on transfer coefficients has been expanded substantially to more closely link job practices to the crop groups as indicated above. It has also more clearly defined the scope of the types of tasks/job functions that should be addressed using these transfer coefficients. The policy also describes which kinds of jobs result in exposures that cannot be addressed with transfer coefficients or those that are of special concern such as vacuuming while harvesting tree nuts. It also describes in more detail those exposures that are considered to be negligible as outlined in HED Exposure SAC Policy 11: *Mechanized Agricultural Practices and Post-Application Exposure Assessments* dated May 1, 2000 (e.g., mechanical harvesting and weeding). It should be noted that mechanical harvesting and other similar low/no exposure activities should be addressed by the guidance contained in Policy 11 which is based on the Worker Protection Standard guidance for such activities (40CFR 170). If there are exposures that are of special concern, then additional data or characterization in the risk mitigation phase of the reregistration process should be considered.

(ii) Occupational Postapplication Exposure Data and Assumptions

Two chemical-specific postapplication studies that provided dislodgeable foliar residue (DFR) data for cabbage and citrus were available. Although the citrus use is not longer supported by the registrant, the data generated in this study can be used as surrogates for other crops. Because of the absence of additional DFR data for the various other crops treated with diazinon, the available DFR data are used as surrogate residue values for other crops using best scientific judgement. Therefore, the assessment of postapplication exposures in this document is based on a grouping of activities associated with various representative crops. The potential for dermal contact during postapplication activities (e.g., harvesting) is assessed using a matrix of potential dermal contact rates by activity and associated crops with groupings shown on **Table 23**. Uncertainties are introduced into the assessment when crop-specific residues are used to estimate residues from other types of crops, however, it is believed to be more realistic than assuming a default initial residue value based on the application rate and an assumed dissipation rate per day.

Transfer coefficients (Tc) are used to relate the leaf residue values to activity patterns (e.g., harvesting) to estimate potential human exposure. Harvesting activities are assessed in this RED using activity-specific transfer coefficients from HED's Exposure Science Advisory Council *Policy #3.1 Agricultural Transfer Coefficients* which includes the newly submitted ARTF data. **Table 23** reports the transfer coefficients used to estimate potential exposure levels for all crops treated with diazinon to determine the margin of exposure (MOE). The transfer coefficient listed in the table is for hand harvesting (unless noted). The transfer coefficients in parentheses are the range of values for the different activities. For example, the low transfer coefficients generally represent low contact activities such as weeding, scouting, and irrigating. High transfer coefficients generally represent activities with more foliar contact such as thinning, hand harvesting, etc.

Table 23
Crop Groupings: Selected Transfer Coefficients, Treated Crops, and Rates

Transfer Coefficient Grouping (a)	Specific Transfer Coefficient (cm2/hr) (b)	Diazinon Specific Crops (c)	Max Foliar Rate (lb ai/acre) (d)
Low berry	1,500 (400 to 1800)	Blackberries, raspberries, blueberries, cranberries, strawberries	1 to 3
Bunch/Bundle	2,000 (100 to 2300)	hops	1

Table 23

Crop Groupings: Selected Transfer Coefficients, Treated Crops, and Rates

Transfer Coefficient Grouping (a)	Specific Transfer Coefficient (cm2/hr) (b)	Diazinon Specific Crops [(c)]	Max Foliar Rate (lb ai/acre) (d)
Field row crop, low & medium	2,500 (100 to 2760)	beans, peas	0.75
Field row crop, tall	17,000 (100 to 25,000)	sweet corn, sorghum	1.25
Field grown nursery crops	7,000 (2400 to 13000)	carnation, chrysanthemum (exposure data are not available for ball/burlap other types of ornamentals such as azalea, boxwood, dogwood, juniper, etc.)	2
Deciduous tree fruit	3000 harvest 8000 thinning	apples, apricots, cherries, figs, nectarines, peaches, pears, plums	2
Nut tree	2500 (200 to 5000)	Walnut foliar treatment (almonds dormant only)	3
Root vegetables	2,500 (140 to 2800)	beets, carrots, onions, parsnips, potatoes, radishes	0.5
Cucurbit vegetables	2,500 (490 to 2800)	cucumbers, melons	0.75
Fruiting vegetables	1,000 (490 to 1900)	peppers, tomatoes	0.75
Brassica vegetables	5,000 (1700 to 7600)	cole crops	0.5
Leafy vegetables	2,500 (490 to 2800)	lettuce, parsley, spinach, swiss chard	0.5
Vine & trellis crops	5,000 harvest 10,000 girdling, cane turning	grapes	1

a DFR data for citrus were used to represent the deciduous tree fruits and tree nuts. The cabbage DFR data were used for all other crop groupings.

b The transfer coefficient listed is for hand harvesting (except where noted). The values listed in parentheses represent other exposure activities such as scouting, weeding, pruning, etc.

c The diazinon treated crops are based on EPA Reg. Nos. 34704-248, 100-460, 9779-210, 100-461, 100-784. The list of diazinon treated crops maybe incomplete; any missing crops can be added to the appropriate category.

d The maximum application rate is based on foliar applications. The higher labeled rates (e.g., 4 lb ai/acre) are for preplant soil incorporated uses. Ornamental rate is assessed for aphids, mites, whiteflies, etc because the transfer coefficient represents cut flowers. Rate assumes 400 gallons/acre. The higher ornamental rate (up to 6 lb ai/acre assuming 400 gallons/acre) is for insects such as webworms and leafrollers on ornamental trees and shrubs.

(iii) Occupational Postapplication Risk Characterization

The results of the short- and intermediate-term postapplication assessments indicate that REIs need to be established. The REIs are presented on **Table 24**. The results of the dermal postapplication assessments for workers exposed to diazinon for most agricultural, and greenhouse activities indicate that MOEs are less than 100 at the current Worker Protection Standard (WPS)-required restricted entry interval (REIs) of 24 hours. Therefore, the majority of postapplication exposures exceed HED's level of concern. The MOEs for postapplication workers did not reach MOEs of 100 for 2-6 days after treatment for most vegetable crops, 3-8 days for fruit trees, 3-9 days for field crops, 3-7 days for berries, 6-8 days for ornamentals and 4-8 days for grapes. The REIs were based exclusively on dermal exposures because potential inhalation exposures were determined to be negligible in comparison. The potential for dermal contact during postapplication activities (e.g., harvesting) is assessed using a matrix of potential dermal contact rates by activity and associated crops. Chemical-specific postapplication exposure Dislodgeable Foliar Residue (DFR) data were submitted for cabbage and oranges. These data were used along with HED standard transfer coefficients to assess potential exposures to workers reentering treated sites. The occupational postapplication assessment is believed to be reasonably representative of diazinon uses, except for nut trees and outdoor ornamental uses, which lack adequate transfer coefficient data. Details of this assessment are presented in memorandum from D. Smegal/T. Leighton to B. Chambliss and D. Drew, November 30, 2000, D270837.

Mushroom houses: No data were submitted in support of postapplication exposures for workers re-entering mushroom houses. EPA has identified potential dermal and inhalation exposures resulting from this indoor application. The Diazinon 50W label (EPA Reg. No. 100-460) directions for mushroom houses is to use a spray dilution rate of 0.04 to 0.05 lb ai/gallon and apply "on outside and inside walls, floors and sideboards of mushroom houses after compost has been pasteurized by heating ... and spray over the plastic covering the beds and trays after spawning." Potential dermal exposures in mushroom houses may arise from workers contacting treated surfaces as all surfaces may be treated. The potential inhalation exposures may result from air concentrations of diazinon in the mushroom house resulting from the application before or after ventilation. Additional data are needed to estimate the potential for dermal exposure in mushroom houses including (1) identification of mushroom house activities that may result in dermal contact, (2) the residue levels on the sideboards and plastic covering the beds and trays, and (3) direct dermal exposure measurements or transfer coefficients. Additional data are also needed to determine air concentrations of diazinon over time. In lieu of air concentration data to calculate exposure/risk, HED determined an allowable air concentration based on the inhalation LOAEL of 0.1 mg/m^3 from a 21-day whole body aerosol study exposing rats 6-hours per day and the uncertainty factor of 300. The estimated 6 hour time-weighted-average (TWA) allowable air concentration is 0.0003 mg/m^3 (i.e., LOAEL of 0.1 mg/m^3 divided by 300 UF). This calculation assumes that the rat and human activity level for a breathing weight is equivalent. The limit of detection (LOD) from the air sampling portion of the diazinon lawn treatment study (MRID 449591-01) is listed as 0.0006 mg/m^3 (see study results in this chapter for actual air concentration levels at specific time intervals).

Uncertainties: The occupational postapplication assessments are believed to be reasonable high end representations of diazinon uses. There are, however, many uncertainties in these assessments. The uncertainties include but are not limited to the following:

- *Crop Specific Residues:* A multitude of crops are treated with diazinon and crop-specific residue data are only available for two crops. Therefore, the use of the available data to "simulate" residues on other crops introduces uncertainties in the setting of restricted-entry intervals. It is reasonable to believe that the residues monitored in the available studies approximate the residues on other crops, but the extent that these residues might be an under- or overestimate is unknown.

- *Extrapolation/Normalization of Residues:* The cabbage and citrus residues were not monitored at the maximum application rate specified on diazinon labels for all foliar treatments. Therefore, the residues were normalized from the rate used in the study (1 lb ai/acre for citrus and 0.5 lb ai/acre for cabbage) to reflect the maximum foliar application rates. Normalizing the residues to the maximum application rate is a standard practice used by HED so as not to underestimate the residues. In most cases the application rates were not extrapolated to such a degree that may significantly overestimate the residues. However, additional refinement of the DFR data for berries, ornamentals, and walnuts at their higher application rates may be warranted.

C *Transfer Coefficients:* The transfer coefficients selected are based on the activities monitored by ARTF. A wide range of transfer coefficients are available and are provided in HED's revised policy for agricultural transfer coefficients (i.e., HED Exposure SAC Policy 3.1: *Agricultural Transfer Coefficients*). The transfer coefficients selected to represent the crop groupings are considered to be in the high end of the range, but not the maximum. A detailed review of the ARTF data has not been completed at this time.

The ornamental diazinon use encompasses flowers (e.g., carnation and chrysanthemum) and other types of ornamentals such as azalea, boxwood, dogwood, juniper, etc. The ARTF is currently conducting studies to assess the exposures involved with ornamental work activities. The assessment of ornamental diazinon use in this document is based on transfer coefficients for cut flowers. This transfer coefficient is based on values obtained from Brouwer et al (1992) as listed in HED's policy on transfer coefficients. Brouwer et al (1992) data are based on greenhouse applications and is being used in this assessment for outdoor grown ornamentals as a high end estimate for all ornamentals. Further refinements to this assessment can be made once the new ARTF data are submitted.

C *Exposure Frequency/Duration:* The amount of time (e.g., days) that a worker would be involved in postapplication activities in diazinon treated fields is not known with certainty. However, based on the exposure duration for short-term exposure being defined as 1 to 7 days, and the intermediate-term duration from 7 days to several months, this postapplication assessment includes both durations. The daily exposures are calculated using the residue level predicted on a specific day after treatment; subsequent declining residue levels (i.e., average residues under the dissipation curve) are not incorporated into the assessment. Therefore, the short-term assessment is protective of workers rotating into freshly treated fields and being exposed to the same DFR level for 1 to 7 days (i.e., 1 to 7 fields at the day the REI expires).

For the intermediate-term assessment, the daily dissipation of residues to reflect a declining worker's exposure over more than a 7 day period was not factored into the assessment because of (1) the lack of information pertaining to exposure frequency/duration of workers in treated fields, (2) harvesters may travel to multiple treated fields thus encountering higher residues in each field, and (3) the time-to-effect is not reported in the 21-day dermal rabbit study. If the number of days a worker was exposed in a treated field could be determined an average residue value could be used in the assessment. The intermediate-term assessment is a conservative approach to setting REIs because declining residues overtime are not factored into the assessment, and therefore, may overstate the daily exposure a worker receives over time. Based on the rapid dissipation of diazinon, the intermediate-term MOEs reported most likely overstate the exposures.

C *Timing of Application:* Many of the diazinon uses involving higher application rates are for preplant soil incorporated uses. MOEs are provided in this assessment only for the foliar applications (e.g., almonds are treated at 3 lb ai/acre as a dormant only application).

C *Children Postapplication Activities (e.g., harvesting and/or bystander)*: GAO (2000) raised the following question in its report, *Pesticides: Improvements Needed to Ensure the Safety of Farmworkers and Their Children* -- How can the current restricted entry intervals (REIs) calculations which are based on body weights be protective of children? This report surmised that "other factors being equal" the lower body weight of a child would extend the REI. However, the dermal dose used to establish REIs is based on several factors in addition to the median adult male/female body weight including the median adult male/female surface area and the transfer coefficient (related to body surface area). The following calculation describes HED's position that the current method to estimate REIs is protective of children 12 years old that are harvesting crops. The 12 year old age was selected from the child labor requirements in agriculture under the Fair Labor Standards Act (FLSA). Exceptions to the FLSA include 10 year olds that are permanent residents that "hand harvest short season crops" and any minors of the farm owner/operator. The quantitative data indicate that the median body surface area (cm^2) to the median body weight (kg) ratio of a 12 year old compared to that of an adult results in a 18 percent underestimate of the child [(((child 13700 cm^2/44 kg) - (adult 18440 cm^2/70 kg)) / (adult 18440 cm^2/70 kg)) x 100]. Historical transfer coefficient data indicate that the higher the productivity of a worker the higher the transfer coefficient. HED believes that it is reasonable to assume that the productivity of a 12 year old is less than that of an adult. HED believes that transfer coefficients for 12 year olds are lower than for adults and that the difference in the magnitude of the transfer coefficient will nullify the 18 percent underestimate attributed to the ratio of body surface area to body weight.

These uncertainties are inherent in most pesticide exposure assessments. The conservative nature of the assessments, however, are believed to be protective of the worker.

Table 24 Summary of "The Days After Treatment" to Reach the Target MOE for Hand Harvesting (a)					
Crop Grouping	**Diazinon Specific Crops**	**Max Foliar Rate (lb ai/acre)**	**Days After Treatment Target MOE Achieved**		**PHI (days)**
			Short-term (Target MOE 100) (b)	**Intermediate-term (Target MOE = 300) (c)**	
Low berry	Blackberries, raspberries, blueberries, cranberries, strawberries	3 (ranges from 1 to 3)	4 to 5 (strawberries @ 1 lb ai/A = 3)	6 to7 (strawberry @ 1 lb ai/A=4 to 5)	5 to 7
Bunch/Bundle	hops	1	3	5	14
Field row crop, low & medium	beans, peas	0.75	3	5	7
Field row crop, tall	sweet corn, sorghum	1.25	7	9	7
Field grown nursery ornamentals	carnation, chrysanthemum (exposure data are not available for ball/burlap other types of ornamentals such as azalea, boxwood, dogwood, juniper)	2	6 to 7	8	12 hr REI
Deciduous tree fruit	apples, apricots, cherries, figs, nectarines, peaches, pears, plums	2	3 to 4 (7 to 8 for thinning)	8 (11 to12 for thinning)	21
Tree nuts	Walnuts (almonds dormant spray only)	3	18	greater than 30	45
Root vegetables	beets, carrots, onions, parsnips, potatoes, radishes	0.5	2 to 3	4 to5	14+
Cucurbit vegetables	cucumbers, melons	0.75	3	5	7

Table 24 Summary of "The Days After Treatment" to Reach the Target MOE for Hand Harvesting (a)					
Crop Grouping	**Diazinon Specific Crops**	**Max Foliar Rate (lb ai/acre)**	**Days After Treatment Target MOE Achieved**		**PHI (days)**
			Short-term (Target MOE 100) (b)	**Intermediate-term (Target MOE = 300) (c)**	
Fruiting vegetables	peppers, tomatoes	0.75	2	3 to 4	1 to 5
Brassica vegetables	cole crops	0.5	3 to 4	5 to 6	7
Leafy vegetables	lettuce, parsley, spinach, swiss chard	0.5	2 to 3	4 to 5	10+
Vine & trellis crops	grapes	1	4 to 5 (6 for girdling, cane turning)	4 to 5 (7 to 8 for girdling, cane turning)	28

(a) Results are for the high end exposure activity of hand harvesting.

(b) Short-term dermal NOAEL = 1 mg/kg/day (21-day rabbit dermal study with a 100 target MOE).

(c) Intermediate-term dermal NOAEL = 1 mg/kg/day (21-day rabbit dermal study with a 300 target MOE).

c. Residential Handler Exposure

Potential diazinon residential handler exposures can result from treatment of turf and ornamental plants, vegetable gardens, as well as indoor use (i.e., for cockroaches, ants, etc). Residential handler exposures to diazinon can occur via dermal and inhalation routes during handling, mixing, loading and applying activities. The registrants have recently agreed (July 2000) to discontinue to support the registration of indoor uses. This includes use inside any structure or vehicle, vessel, or aircraft and/or on any contents therein. Therefore, potential exposures and risks to residential handlers are not assessed for indoor uses of diazinon.

(i) Residential Handler Exposure Scenarios

Diazinon has a wide variety of outdoor residential uses including lawn and ornamental treatments, spot treatments, use on vegetable gardens and around the house perimeter. The current registered labels permit residents to mix/load/apply both liquid and granular formulations at rates up to 4 and 4.4 lb a.i. per acre, respectively up to 4 or more times per year. Some labels do not specify a limit on number of applications, or state apply as needed. Diazinon is applied by many methods including spray equipment (hose-end sprayer, handwand), and granular spreaders. Residential handlers may receive dermal and inhalation exposure to diazinon when mixing, loading and applying. All residential handler use patterns are considered to result in short-term (1-7 day) exposures.

HED evaluated the following six residential handler exposure scenarios resulting from diazinon's registered uses:

(1) Mixing/loading/applying liquids with a low pressure handwand (spot treatment);
(2) Mixing/loading/applying liquids with a backpack sprayer (spot treatment);
(3) Mixing/loading/applying liquids with a ready-to-use (RTU) hose-end sprayer;
(4) Mixing/loading/applying liquids with a conventional garden hose-end sprayer;

(5) Loading/applying with a push-type spreader; and

(6) Loading/applying granules with a belly grinder (spot treatment).

In July 2000, Novartis stated that they do not plan to support the belly grinder and airless sprayer methods of application. However, HED included the belly grinder analysis for completeness, since the labels have yet to be modified to reflect this change.

(ii) Residential Handler Exposure Data Sources and Assumptions

The registrant submitted one chemical-specific handler study that assessed three residential handler application scenarios, which was utilized to the greatest extent possible. This study conducted both biomonitoring (i.e., urinary measurement of a unique diazinon metabolite, G-27550, following exposure) and/or passive dosimetry measurements on 42 different residential applicators. In addition, passive dosimetry exposure data from a recently submitted Occupational and Residential Exposure Task Force (ORETF) handler study was used. This study assessed residential handler exposures to diazinon resulting from a conventional hose-end sprayer (dial type sprayer) and a ready-to-use hose-end sprayer (MRID 44972201). In this study, residents treated 5,000 ft^2 of lawn at the maximum application rate of 4 lb ai/acre diazinon, resulting in a total of 0.5 lb ai handled per replicate. The same ORETF study (MRID 44972201) assessed residential handler exposures to dacthal resulting from a granular push-type spreader. This study was used as a surrogate to assess diazinon, where the residents treated 10,000 ft^2 of lawn at a typical rate of 2 lb ai/acre, resulting in a total of 0.45 lb ai handled per replicate. In the absence of chemical-specific data, HED relied on information from the Draft Residential Standard Operating Procedures (SOPs - December 1997), and updated assumptions (2000 SOPs). The Residential SOPs were used to assess the backpack sprayer and the belly grinder exposure scenarios. The residential unit exposure numbers are derived from the Pesticide Handler Exposure Database (PHED) Version 1.1. Dermal Unit Exposures are based on homeowner applicators wearing short sleeve shirts and short pants, and no gloves (sss, sp, ng) open mixing/loading; except for backpack sprayers. Chemical resistant gloves are included for the backpack assessment because the "no glove" scenario is not available for hands. To account for the "no glove" scenario, a back calculation was conducted using a 90% protection factor to obtain the appropriate unit exposure value for a no glove scenario for backpack application. Unit inhalation exposure estimates assume no respirator.

The following assumptions (which include *current* HED standard values) were used to calculate inhalation exposures.

* For the liquid exposure assessments, the maximum application rate from Ortho® Diazinon Ultra™ (EPA Reg # 239-2643, Liquid water base concentrate, 22.4% ai) of 4 lbs. ai/acre was assumed.

* For the granular exposure assessment, the maximum application rate from Ortho® Diazinon Soil and Turf ™ (EPA Reg # 239-2479, granular, 4.84 % ai) of 4.4 lbs. ai/acre was assumed.

* For the liquid formulation, handlers were assumed to be using a low-pressure hand wand for spot treatments to 1,000 ft^2 areas or a conventional or ready-to-use (RTU) garden hose-end sprayer for broadcast to a 0.5 acre lawn. The 0.5 acre value is the standard HED-recommended assumption and represents the mean to upper-percentile range of the distribution of lawn size. Recent lawn size survey data suggest that up to 0.5 acre represents 73% of the 2,300 respondents, while nearly 16% of the respondents had lawn sizes that ranged from 0.57 to 1 acre (Outdoor Residential Use and Usage Survey and National Gardening Association Survey 1999). In this survey, only 2,300 respondents of 4,100 knew the size of their lawns.

* Handlers using the granular formulation were assumed to be using a 'push type' granular spreader to treat a lawn size of 15,000 ft^2 (0.344 acre), and a belly grinder for spot treatments to 1,000 ft^2 areas. Some granular labels state that residents should only treat 15,000 ft^2 per day (0.344 acre)(EPA Reg # 100-468). HED notes, however, that some labels currently do not restrict the area treated (EPA Reg 3239-2479), and these labels should be modified to add such a restriction.

* The Residential SOP/PHED dermal unit exposures for the backpack sprayer and the belly grinder are 5.1 and 110 mg/lb ai handled, respectively. The Residential SOP/PHED inhalation unit exposures for the backpack sprayer and the belly grinder are 0.03 and 0.062 mg/lb ai handled, respectively. These values are from Appendix B of the 1997 Draft SOPs for Residential Exposure Assessments. As noted previously, the chemical-specific dermal and inhalation unit exposures are central tendency estimates based on the distribution of the data set (i.e., geometric mean for lognormal data sets, arithmetic mean for normal data sets and median for other data distributions).

* Residential handler weight is 70 kg.

C The overall estimate of dermal and inhalation exposure is believed to represent central to high-end values for the 0.5 acre treatment area.

Chemical-specific dermal and inhalation exposure estimates from the passive dosimetry measurements, and absorbed dose estimates from biomonitoring data were also used to the greatest extent possible. Biomonitoring data are available for three scenarios: (1) low pressure handwand, (2), ready-to-use hose end sprayer and (3) conventional hose-end sprayer (MRID 45184305). HED reviewed this study in a memorandum from D. Smegal to B. Chambliss/D. Drew, November 2000, D268247. In this study, the unique metabolite of diazinon, G-27550, was measured in urine for 2-3 days following exposure. In evaluating the biomonitoring data, both the central-tendency (i.e., geometric mean or arithmetic mean) and the 90th percentile absorbed diazinon dose estimate were used to estimate exposure and risks. The 90th percentile values are presented because the biomonitoring data represent measured exposures to individuals and are not extrapolated using high-end assumptions. As shown on **Table 25**, biomonitoring studies had residents handling 4 gallons of product (0.021 lb ai per replicate) for handwand or 0.5 lb ai per replicate for the hose-end sprayer to treat 5000 ft^2. HED typically evaluates exposures for 0.5 acre or 21,800 ft^2 for the hose-end sprayer. The hose-end sprayer biomonitoring data for 5,000 ft^2 will underestimate exposure to individuals treating larger lawns. The results are reported for the 5,000 ft^2 treatment area because that was consistent with packaging size and it was also the area treated in the registrant study. HED notes that diazinon is packaged in 1 quart ready-to-use containers that treat 5,000 ft^2. To treat larger lawns, additional packages would have to be purchased. HED also extrapolated the biomonitoring data using the mean results to 0.5 acre to be consistent with current HED-policy.

(iii) Residential Handler Risk Characterization

A summary of the short-term risk estimates for residential handlers is presented on **Table 25**. MOEs for residential handlers were derived by dividing the appropriate short-term NOAEL or LOAEL, shown on **Table 2**, by the daily short-term dermal or inhalation exposure estimate. As noted previously, the short-term dermal NOAEL of 1 mg/kg/day is from a dermal rabbit study, and therefore, no dermal absorption adjustment is necessary. For inhalation, the short-term LOAEL is 0.026 mg/kg/day based on a whole body rat inhalation study. The biomonitoring data exposure estimates were compared to the short-term oral NOAEL of 0.25 mg/kg/day. An oral NOAEL was selected in the absence of an absorbed dermal NOAEL, as the majority of exposure is via the dermal route. The target MOE is 100 for handler short-term dermal residential exposures to diazinon, and also for the biomonitoring exposure estimates. For residential handler inhalation exposures of any duration, the target MOE is 300. MOEs below this level would represent a risk concern.

As noted previously for occupational handlers, HED estimated total dermal and inhalation risk using an aggregate risk index (ARI) because of different target MOE for dermal (MOE=100) and inhalation (MOE=300) exposure routes. The target ARI is $\geq$1 (i.e., ARIs less than 1 would exceed HED's level of concern).

Exposure and risk estimates for the residential handler scenarios are shown on **Table 25.** Estimated risks, expressed as MOEs, for all residential handler scenarios are less than 100 for dermal and 300 for inhalation based on unit exposures from passive dosimetry data, except for inhalation MOEs for the push-type spreader scenario (MOE=1,300). Therefore, these scenarios exceed HED's level of concern. HED also evaluated residential handlers wearing long pants for the push-type granular spreader. As shown on **Table 25**, the dermal MOEs for this scenario with short pants and long pants are 68 and 520, respectively, indicating that the majority of the dermal exposure is to the lower legs. HED policy is to assume residents wear short pants because it is difficult to enforce clothing requirements for homeowners. HED notes that current diazinon granular labels (EPA Reg No. 239-2479, 100-468) do not recommend applicators wear long pants.

Biomonitoring data were also available for three scenarios: (1) low pressure handwand, (2) ready-to-use hose end sprayer, and (3) and conventional hose-end sprayer (MRID 45184305). As shown on **Table 25**, the MOEs based on central tendency and 90th percentile exposure estimates as measured in the study (i.e., 5,000 ft^2) are greater than 100, and therefore do not exceed HED's level of concern, except for the 90th percentile conventional hose-end sprayer (MOE=27). However, the geometric mean biomonitoring exposure estimates for the ready-to-use hose-end sprayer or the conventional hose-end sprayer extrapolated to 0.5 acre result in MOEs less than 100, and therefore, exceed HED's level of concern. These MOEs represent total exposure, because they are based on a total absorbed dose resulting from primarily dermal and inhalation exposure.

As shown on **Table 25**, all the ARIs are less than 1, and therefore exceed HED's level of concern for residential handlers, except for residents wearing long pants during granular application with a push type spreader to 0.34 acres (ARI=2.4). These ARIs range from 0.03 for the liquid conventional hose end sprayer assessment using the ORETF data to 0.89 for the backpack sprayer using the Residential SOPs/PHED unit exposure estimates. It should be noted that HED has more confidence in the chemical-specific exposure and risk estimates for the low-pressure handwand (ARI=0.38-0.25) than the exposure and risk estimates based on low quality data available for the surrogate data from PHED (e.g., back calculating a no glove scenario using a protection factor, 11 replicates, and C grade data). The PHED data may underestimate exposure and risks due to the relatively high volatility of diazinon (vapor pressure of 1.4×10^{-4} mmHg) relative to the chemical surrogate data in PHED.

Uncertainties: As noted previously, all risk assessments involve the use of assumptions, judgement and available reliable data to varying degrees. Often, the available data are not the ideal data for evaluating potential exposure scenarios. This results in uncertainty in the numerical estimates of risk. Consideration of the uncertainty inherent in the risk assessment process permits better evaluation of the risk assessment and understanding of the possible human health impacts. Risks estimates may be overestimated or underestimated to varying degrees. The most significant uncertainties are discussed below.

As mentioned previously, the diazinon-specific biomonitoring results may underestimate exposure and risk. While biomonitoring data are typically preferred for assessing exposures, HED believes the biomonitoring results for diazinon may underestimate exposure and risk primarily due to:

(1) Possible incomplete urine collection for some individuals (at least 9 of 42 individuals appeared to have low urine volumes). Creatinine measurements were not provided to assist in the determination of complete urine collection.

(2) There is a lack of pharmacokinetic data for the G-27550 metabolite following dermal and inhalation exposure. HED estimated biomonitoring doses assuming the urinary metabolite G-27550 represents 7.9% of diazinon exposure based on a human oral pharmacokinetic study, which may not reflect dermal or inhalation exposures.

For these two reasons, Pest Management Regulatory Agency (PMRA) in Canada does not consider the biomonitoring results to be acceptable for use in generating handler exposure estimates (personal communication with Kristen Macey, 11/21/00).

(3) The biomonitoring risk estimates are based on residents handling 0.5 lb ai per replicate for hose-end sprayer to treat 5000 ft^2, while HED typically evaluates a 0.5 acre or 21,800 ft^2 lawn treatment for the hose-end sprayer.

(4) Biomonitoring results (based on dermal and inhalation exposure) are compared to the short-term oral NOAEL of 0.25 mg/kg/day to calculate MOEs. HED notes that the short-term inhalation LOAEL of 0.026 mg/kg/day is at least 10 times lower than the oral NOAEL. There are significant uncertainties in comparing biomonitoring data resulting from dermal and inhalation exposure to oral toxicity data because of differences in pharmokinetics and toxicity for the routes of exposure. HED believes it is inappropriate to compare the total absorbed dose to the inhalation LOAEL because most of the exposure is via the dermal route. In addition, the available dermal absorption data are variable and do not allow adjustment of the dermal NOAEL of 1 mg/kg/day to an absorbed dose (i.e., dermal absorption ranges from <1 to 58% depending on individual, and equipment type based on MRID 45184305).

A factor that may contribute to the possible over-estimation of risk is that a 21 day inhalation endpoint based on whole body exposure in rats, and a 21 day dermal endpoint in rabbits were used to assess a short-term (often single day) exposure scenario.

Table 25 Short-Term Residential Handler Exposure and Risk Estimates										
Exposure Scenario (Scen. #)	**Data Source**	**Dermal Unit Exposure (mg/lb ai) (a)**	**Inhalation Unit Exposure (mg/lb ai) (b)**	**Application Rate (lb ai/acre) (c)**	**Amount Handled per Day or Area Treated (d)**	**Daily Dose (mg/kg/day)**		**MOE**		**Aggregate Risk Index (ARI) (l) (1 needed)**
						Dermal (e)	**Inhalation (f)**	**Dermal (g)**	**Inhalation (h)**	
Mixing/Loading/Applying Liquids										
Liquid Low Pressure Handwand (1)	Novartis Study (MRID 45184305)	12.38 (G.M.) passive dosimetry	0.159 (G.M.) passive dosimetry	4	1000 ft^2 (0.023 acre)	0.016	0.00021	**62**	**130**	**0.25**
		Biomonitoring (see Dose estimates) (n-13)			0.021 lb ai (4 gallons)	0.00075 (A.M.) 0.0014 (90^{th} percentile) (total absorbed dose from biomonitoring study)		330 (A.M.) 180 (90^{th} percentile) (total dose) (i)		NA
Backpack Sprayer (2)	Residential SOPs/PHED	5.1 (j)	0.03 (j)	4	1000 ft^2 (0.023 acre)	0.007	0.0004	150	660	**0.89**
Liquid Ready-to-Use Garden Hose End Sprayer (3)	Novartis Study (MRID 45184305)	1.58 (G.M) (n=11) passive dosimetry	0.0457 (G.M) (n=11) passive dosimetry	4	0.5 acres	0.045	0.00131	**22**	**20**	**0.051**

Table 25
Short-Term Residential Handler Exposure and Risk Estimates

Exposure Scenario (Scen. #)	Data Source	Dermal Unit Exposure (mg/lb ai) (a)	Inhalation Unit Exposure (mg/lb ai) (b)	Application Rate (lb ai/acre) (c)	Amount Handled per Day or Area Treated (d)	Daily Dose (mg/kg/day)		MOE		Aggregate Risk Index (ARI) (l) (1 needed)
						Dermal (e)	Inhalation (f)	Dermal (g)	Inhalation (h)	
		Biomonitoring (see Dose estimates) (n=15)			5,000 ft^2 (0.11 acre)	0.00061 (G.M.) 0.0022 (90^{th} percentile) (total absorbed dose from biomonitoring study)		410 (G.M.) 110 (90^{th} percentile) (total dose) (i)		NA
					0.5 acres	0.00266 (extrapolated from G.M.)		**94**		NA
	ORETF Diazinon Study (MRID 44972201)	2.6 (G.M.) (n=30) passive dosimetry	0.011 (G.M.) (n=30) passive dosimetry	4	0.5 acres	0.074	0.00031	**13**	**83**	**0.09**
	Combined Data from Novartis and ORETF Studies	2.3 (G.M.) 33 (max) (n=41) passive dosimetry	0.016 (G.M.) 0.16 (max) (n=41) passive dosimetry			0.066	0.0046	**15**	**57**	**0.084**
Liquid Conventional Hose End Sprayer (4)	Novartis Study (MRID 45184305)	4.68 (G.M.) (n=12) passive dosimetry	0.0114 (G.M.) (n=11) passive dosimetry	4	0.5 acres	0.134	0.00033	**7**	**80**	**0.058**

Table 25 Short-Term Residential Handler Exposure and Risk Estimates										
Exposure Scenario (Scen. #)	**Data Source**	**Dermal Unit Exposure (mg/lb ai) (a)**	**Inhalation Unit Exposure (mg/lb ai) (b)**	**Application Rate (lb ai/acre) (c)**	**Amount Handled per Day or Area Treated (d)**	**Daily Dose (mg/kg/day)**		**MOE**		**Aggregate Risk Index (ARI) (l) (1 needed)**
						Dermal (e)	**Inhalation (f)**	**Dermal (g)**	**Inhalation (h)**	
		Biomonitoring (see Dose estimates) (n=14)			5,000 ft ^{2} (0.11 acre)	0.00096 (G.M.) 0.0092 (90th percentile) (total absorbed dose from biomonitoring study)		260 (G.M.) **27 (90th percentile)** (total dose) (i)		NA
					0.5 acres	0.0042 (extrapolated from G.M.)		**60**		NA
	ORETF Diazinon Study (MRID 44972201)	10.9 (G.M.) (n=30) passive dosimetry	0.016 (G.M.) (n=29) passive dosimetry		0.5 acres	0.311	0.00046	**3**	**57**	**0.03**
	Combined Data from Novartis and ORETF Studies	8.6 (G.M.) 49 (max) (n=42) passive dosimetry	0.015 (G.M.) 0.089 (max) (n=40) passive dosimetry			0.246	0.00043	**4**	**61**	**0.034**

Table 25 Short-Term Residential Handler Exposure and Risk Estimates										
Exposure Scenario (Scen. #)	**Data Source**	**Dermal Unit Exposure (mg/lb ai) (a)**	**Inhalation Unit Exposure (mg/lb ai) (b)**	**Application Rate (lb ai/acre) (c)**	**Amount Handled per Day or Area Treated (d)**	**Daily Dose (mg/kg/day)**		**MOE**		**Aggregate Risk Index (ARI) (l) (1 needed)**
						Dermal (e)	**Inhalation (f)**	**Dermal (g)**	**Inhalation (h)**	
Loading/Applying Granules										
Granular Loading/-Applying with a Push Type Spreader (5)	ORETF Study with Dacthal (MRID 44972201)	0.68 (G.M) (max 7.9) (shorts, short sleeved shirt, no gloves)	0.00091 (G.M.)	4.4 (maximum)	0.344 acres (15,000 ft^2)	0.015 (G.M)	0.00002 (G.M)	**68**	1,300 (G.M.)	**0.59 (G.M)**
		0.089 (G.M) (0.52 max) (long pants, short sleeved shirt, no gloves)				0.002		520		2.4
Granular (Belly Grinder) (6)	Residential SOPs/PHED	110 (k)	0.062 (k)	4.4 (maximum)	1,000 ft^2 (0.023 acre)	0.159	0.00009	**6.3**	**290**	**0.059**

NA = Not applicable

G.M. = Geometric mean

A.M = Arithmetic mean

(a) Dermal unit exposure from chemical-specific studies based on geometric mean for lognormally distributed data sets or the arithmetic mean for normally distributed data sets. Otherwise, dermal unit exposure were values from Residential SOPs draft December 1997/PHED. Baseline dermal exposure assumes short pants, short sleeved shirt, and no gloves clothing scenario.

(b) Inhalation unit exposure from chemical-specific studies based on geometric mean for lognormally distributed data sets or the arithmetic mean for normally distributed data sets. Inhalation unit exposure values from PHED are from Residential SOPs draft December 1997 (no respirator).

(c) Application rate is based on the Registrant Study, MRID #449591-01, and the labels, Ortho® Diazinon Ultra™ (EPA Reg # 239-2643, Liquid water base concentrate, 22.4% ai, application rate = 4 lbs. ai/A), Ortho® Diazinon Soil and Turf ™ (EPA Reg # 239-2479, granular, 4.84 % ai, application rate = 4.4 lbs. ai/A).

(d) Amount handled per day values are EPA estimates of acreage treated found in the Residential SOPs draft December 1997.Two lawn sizes were evaluated for push-type spreader based on the labels. One label (EPA Reg # 100-468) restricts the area treated to 15,000 ft^2 (0.344 acre), however another label (EPA Reg # 239-2479) does not limit the lawn treatment area, and therefore the HED standard default value of 0.5 acres was assessed.

(e) Dermal daily dose (mg/kg/day) = daily unit exposure (mg/lb ai) x application rate (lb ai/acre) x amount handled per day (acres) / body weight (70 kg).

(f) Inhalation daily dose (mg/kg/day) = inhalation unit exposure (µg/lb ai) x application rate (lb ai/acre) x amount handled per day (acres) x conversion factor (1 mg/1,000 µg) / body weight (70 kg).

(g) Dermal MOE = dermal NOAEL (1 mg/kg/day) / daily dose (mg/kg/day).

(h) Inhalation MOE = LOAEL (0.026 mg/kg/day) / daily dose (mg/kg/day).

(i) Biomonitoring results based on residents handling 4 gallons of product (0.021 lb ai per replicate) for hand wand or 0.5 lb ai per replicate for hose-end sprayer. Dose is estimated assuming that the urinary metabolite G-27550 represents 7.9% of diazinon exposure. This estimate is from a human oral pharmacokinetic study, and does not reflect dermal or inhalation exposures. In the absence of reliable dermal absorption data, the total absorbed dose is compared to the short-term oral NOAEL of 0.25 mg/kg/day. There are significant uncertainties in comparing biomonitoring data resulting from dermal and inhalation exposure to oral toxicity data because of differences in pharmokinetics and toxicity for the routes of exposure.

(j) Dermal unit exposure for the backpack sprayer has low confidence, 8-9 dermal replicates of grades ABC data and 23 hand replicate data of ABC grades. The inhalation unit exposure has high confidence, and 40 replicates of AB grade data.

(k) Dermal unit exposure for the belly grinder has medium confidence, 20-45 dermal replicates of grades ABC data and 70 hand replicate data of all grades. The inhalation unit exposure has medium confidence, and 80 replicates of ABC grade data.

(l) Aggregate Risk Index (ARI) = $MOE_{calculated}$ / $MOE_{acceptable}$ where ARI_{dermal} = $MOE_{calculated\ dermal}$ / $MOE_{acceptable\ dermal,}$ $ARI_{inhalation}$ =

$MOE_{calculated\ inhalation}$ / $MOE_{acceptable\ inhalation}$, and ARI (total) = $1 / (1/ARI_{dermal} + 1/ ARI_{inhalation})$

d. Residential/Recreational Postapplication Exposures and Risks

EPA has determined that there are potential postapplication exposures to residents/individuals entering treated areas both indoors following residential/commercial/institutional treatment (i.e., homes, schools, day care centers, etc) for cockroaches, or other insects and outdoors following turf treatment (i.e., homes, schools, parks, playgrounds, ball fields, etc). In addition, there is a potential for inadvertent oral exposure to children from eating diazinon-treated soil, grass and/or granules, or placing their fingers in their mouths. For residential postapplication activities, the exposure duration is expected to be short-term (1 to 7 days), except pet collar use, which is considered to be potentially long-term. Details of this assessment are presented in a memorandum from D. Smegal/T. Leighton to B. Chambliss and D. Drew, November 30, 2000, D270837.

(i) Postapplication Exposure Scenarios

Potential residential postapplication exposures may occur as a result of turf treatment by residents or professional lawn care operator (LCOs). Specifically, adult and child exposures were evaluated as a result of both liquid and granular diazinon lawn treatments that could occur in both residential and recreational settings (i.e., parks, playgrounds). Adults and children may be exposed to diazinon from dermal contact with treated turf and from inhalation of airborne concentrations. Toddlers may also receive short-term oral exposure from hand-to-mouth and object to mouth activities and from incidental ingestion of soil or pesticide granules during post-application activities. HED also evaluated inhalation and dermal exposures resulting from indoor crack and crevice use, and dermal exposure from pet collar use. As noted previously, the registrant agreed in July 2000 to cancel all indoor uses of diazinon. Nevertheless, the assessments are provided for completeness.

All exposures were assumed to be of short-term duration (1-7 days), except pet collar use, which was considered to be potentially long-term. HED evaluated the following 9 postapplication exposure scenarios associated with liquid and granular turf treatment and indoor uses:

(1) Dermal absorption of diazinon residues on treated turf (adults and children);

(2) Incidental ingestion of diazinon residues resulting from hand to mouth activities on treated turf (children);

(3) Incidental ingestion of diazinon residues resulting from object to mouth activities on treated turf (i.e., turf mouthing) (children);

(4) Incidental ingestion of diazinon residues resulting from soil ingestion (children);

(5) Ingestion of diazinon granules on treated turf (children);

(6) Inhalation of airborne diazinon residues above treated turf (adults and children),

(7) Inhalation of airborne diazinon residues following crack and crevice treatment (adults and children);

(8) Dermal absorption of diazinon residues following crack and crevice treatment (children); and

(9) Dermal absorption of diazinon residues from fur of pets wearing pet collars (adults and children).

HED is in the process of revising the Residential Exposure Assessment SOPs. This process may identify specific areas of further concern with respect to diazinon and exposure to the general population. For example, some of the secondary exposure pathways that EPA is currently examining include exposures resulting from residue tracked into homes from outdoor use, indoor dust, spray drift, exposures to farm worker children; and exposures to children in schools. Currently, there are no methods available to evaluate these potential exposure pathways. These scenarios however, may be evaluated in the future pending revisions to the residential SOPs.

(ii) Data Sources and Assumptions for Postapplication Exposure Calculations

Lawn Treatment

The post-application lawn assessment is based primarily on chemical-specific data from the turf transferable residue (TTR) study submitted by the registrant, Novartis, in December 1999 (MRID 44959101). This study measured TTRs and air concentrations on the day of lawn treatment for both granular and liquid formulated products.   This study is discussed below in more detail. Other chemical-specific studies submitted by the Registrant were reviewed and considered of insufficient quality for risk assessment (MRIDs 40204901, 42063301). In addition, HED relied on generic assumptions as specified by the newly proposed Residential SOPs (2000) and recommended approaches by HED's Exposure Science Advisory Committee (ExpoSAC) to assess children contacting recently treated turf. The SOPs use a high contact activity based on the use of Jazzercise® to represent the exposures of an actively playing child. The proposed assumptions are expected to better represent residential exposure and are still considered to be high-end, screening level assumptions. HED management has authorized the use of the revised residential SOPs that were presented to the FIFRA Scientific Advisory Panel (SAP) in September 1999. Therefore, HED has deviated from the current Residential SOP assumptions and uses the proposed assumptions to calculate exposure estimates.

The exposure estimates for granular and liquid formulations are based on the maximum application rate of 4.4 lbs ai/acre and 4 lbs ai/acre, respectively. BEAD estimates that approximately 4 lb ai/acre is also the average rate for turf treatment by LCOs and in parks and other recreational areas, although the typical application rate for school playing fields is 2.4 lb ai/acre (memo from A. Halvorson, Quantitative Usage Analysis (QUA) for Diazinon, January 1, 1999).

The following chemical-specific study was submitted by the registrant and reviewed by HED in memo from J. Cruz to B. Chambliss and C. Eiden, March 15, 2000 (D229848, D240464, D246141, and D261475):

<u>Turf Study MRID # 449591-01</u>

This 1999 study was conducted in response to an EPA Special Data Call In Notice (March 3, 1995, and February 1998 amendment) for Residential Re-Entry Exposure. Novartis conducted the diazinon turf transferable residue (TTR) and dissipation study in three different states; which are Georgia, California, and Pennsylvania. This study was also conducted in accordance with EPA, FIFRA Good Laboratory

Practice Standards (GLP) 40 CFR Part 160 (October, 1989), and was designed to meet all the requirements of the Agency's Pesticide Assessment Guidelines, Subdivision K, Exposure, Series 132-1 (a) (Series 875- Occupational and Residential Exposure Test Guidelines, 875.2100). The test protocol template was developed by the Outdoor Residential Exposure Task Force (ORETF) for use by Task Force member companies when conducting turf transferable residue studies. The turf transferable method used in this study is called the Modified California Roller Method, which was selected by the ORETF. The two primary formulations of diazinon that are used in the residential market are the granular and the liquid. The Water-Based Concentrate (WBC) was developed to reduce the odor associated with the solvent-based emulsifiable concentrate, which is being phased out of the market place.

TTR data were collected when the turf was dry at 4, 8, 24 and 48 hours postapplication. The air samples were collected three feet above the treated turf at 0-2, 2-4 and 4-8 hour intervals. Four cloth samples, and four air samples were collected per interval per geographic location. The quality of the data were good for the TTRs, and the ambient airborne samples. The air concentrations represent aerosol and particulate levels since no vapors were detected in the 0-2 hour sampling interval. HED has requested vapor residue data from the registrant beyond 2 hours postapplication because it is likely that vapors would not be detected until the turf has dried, approximately 1-2 hours postapplication.

HED evaluated this study and has derived environmental concentrations for use in assessing postapplication exposures and risks to adults and children (1-6 yrs). **Table 13** presents the TTRs, dislodgeable foliage residue, soil residue and air concentrations based on this study. The TTR and air concentrations are presented for each geographic location, and as an average across locations. The values for each location represent an average of 4 samples. The average air concentrations per time interval (0-2, 2-4 and 0-4 hours) are also presented by location. As shown on **Table 13** diazinon air concentrations were below the limit of detection following granular treatment in Georgia and California up to 4 hours after application. However, some air concentrations increased slightly in California 4-8 hours postapplication for non-irrigated granular treated turf (3 to 4 fold increase over 0-2 hour levels). In addition, the air concentrations decrease with time following liquid turf treatment, with levels either non-detectable or 2 to

10 times lower than initial concentrations by 8 hours postapplication. Generally, the air concentrations were lower for irrigated turf then for non-irrigated turf treated with the liquid or granular formulated products. For the granular treatment, two locations (Georgia and California) had non-detectable air residues for both irrigated and non-irrigated lawns up to 4 hours after treatment, while in Pennsylvania, irrigation appeared to reduce air levels to non-detectable levels. The granular labels require watering the lawn following application, although the liquid labels recommend watering the lawn either prior to treatment (for above ground pests) or following treatment (for underground pests) depending on the pest of concern.

For inhalation, HED assessed a 0-2 hour time interval because it is possible that a child or adult could enter the treated turf during or immediately after application. HED also evaluated exposures and risks associated with 2-4 hour and 0-4 hour average air concentrations to address the Registrants comments, and to provide a range of possible inhalation risk estimates that could result from turf treatment. It is likely that individuals will not be on turf treated with liquid formulations until after it has dried, which is usually 1-2 hours following application.

<u>Dermal and Incidental Oral Exposure Assumptions</u>:

The exposure estimates for the dermal and incidental oral pathways are presented on **Table 14**. The following assumptions which are based on *current* HED standard values were used to calculate dermal and oral exposures for diazinon applied to turf:

* Application rate of 4 lb ai/acre for liquid formulated products (EPA Reg #239-2643) and application rate of 4.4 lb ai/acre for granular formulated products (EPA Reg # 239-2479), which represent both the maximum and average rates based on BEAD (QUA memo from A. Halvorson, 1-29-99).
* The turf transferable residues (TTR) were obtained from a diazinon-specific study (MRID 4459101) and used to assess dermal exposures only.

* The transfer coefficients (TC) are 14,500 and 5,200 cm^2 for adults and children, respectively based on Jazzercise data (updated assumption to Residential SOPs 2000). These TCs represent individuals wearing short pants, short sleeved shirts and occasionally footwear.
* The fraction of ai available for transfer to hands from foliage is 0.05 (5%) or the amount applied based on current HED ExpoSac Policy (minute meeting notes, 9/14/2000). The TTR value of 0.049% based on turf treatment with a liquid formulation (MRID 44959101) was not used because the methodology used to obtain a TTR value is not appropriate for assessing "wet or sticky" hands of children, and could underestimate incidental oral exposures to children. The TTR data are designed to assess dermal exposure to pesticides using the choreographed activity Jazzercise, measured on dry cotton dosimeters, and do not address the transferability of residues by hands wetted with saliva. The 5% transfer factor is based on data by Clothier (1999). Dislodgeable foliar residue data from a 1984 California study (MRID 40202901) based on washing grass clippings report average DFRs of 0.8% to 5.7% depending on the methodology.
* Hand surface area is 20 cm^2 which represents the mean palmar surface area of 3 fingers on a toddler (updated assumption to Residential SOPs 2000).
* The saliva extraction factor 0.5 (50%)(updated assumption to Residential SOPs 2000).
* The frequency of oral hand-to-mouth exposure events is assumed to be 20 events/hr for short-term exposure (updated assumption to Residential SOPs 2000).
* The exposure time is assumed to be 2 hrs/day. This is based on the 95th percentile value (i.e., 121 minutes) for playing on grass for ages 1-4 years (Draft Residential SOPs December 18, 1997).
* The ingestion rate for grass and soil are assumed to be 25 cm^2/day (i.e., 2.x2 inches or 4 in^2) and 100 mg/day, respectively (Draft Residential SOPs December 18, 1997). The surface area for grass is intended to represent the approximate area from which a child may grasp a handful of grass or mouth an object such as a toy. HED believes this represents an upper-percentile value. The soil ingestion value is the mean soil ingestion rate for children 1-6 years.
* The body weights are assumed to be 70 and 15 kg for adults and children, respectively (Draft Residential SOPs December 18, 1997).
* The overall estimate of dermal and oral exposure represents central to high-end values.

Incidental Ingestion of Pesticide Granules:

The ExpoSAC recommended that oral exposures among toddlers from incidental ingestion of pesticide granules that have been applied to lawns be calculated in addition to the oral exposure from hand-to-mouth contact. The SAC also suggested that the granular ingestion scenario be considered an individual episodic event that should not be aggregated with other non-dietary or dietary exposure scenarios. HED conducted a screening level assessment of oral exposure for dry pesticide materials that may be ingested by toddlers that play in treated areas. No information regarding the granular size was available. The following assumptions were used to estimate the daily oral dose:

* The assumed ingestion rate for dry pesticide formulations (i.e., pellets and granules) is 0.3 gram/day for children (age 3 years). This is based on the assumption that if 150 pounds of product were applied to a ½-acre lawn, the amount of product per square foot would be approximately 3 g/ft^2, and a child would consume one-tenth of the product available in a square foot. This is believed to be an upper-percentile assumption.
* Toddlers (age 3 years), used to represent the 1 to 6 year old age group, are assumed to weigh 15 kg. This is a mean of the median values for male and female children.
* Ortho® Diazinon Soil and Turf ™ (EPA Reg # 239-2479, Granular) contains 4.84 % ai. Therefore, it was assumed that Fraction, F = 0.0484.
* The dose estimates generated using this method are based on some central tendency (i.e., body weight) and some upper-percentile assumptions (i.e., ingestion rate of dry pesticide formulation, and maximum application rate for short-term assessments) and are considered to be representative of high-end exposures. The uncertainties associated with this assessment stem from the use of an assumed ingestion rate of dry pesticide formulation. The dose estimates are considered to be reasonable high-end estimates.

Inhalation Exposure Assumptions:

The inhalation exposure estimates are presented on **Table 14**. The following assumptions were used to estimate the daily inhalation dose:

* The air concentrations from the chemical-specific study (MRID 44959101) for the 0-2 and 2-4 hour concentrations were evaluated, in addition to the 0-4 hour average. Both the 0-2 and 0-4 hour concentrations were evaluated to assess children that may wander onto treated lawns before they have dried.
* The geographic average air concentration was evaluated for liquid turf treatment. For granular turf treatment, inhalation risks were not assessed following lawn irrigation because all air concentrations were non-detectable. For non-irrigated granular lawn treatment, only Pennsylvania was assesssed because air concentrations were non-detectable in California and Georgia.
* The hourly inhalation rate for adults of 1 m^3/hr for light activities is the value recommended by USEPA Exposure Factors Handbook, pg 5-24. For young children (1-6 years of age), a ventilation rate of 0.7m^3/hr was used. This value is based on data for play and walking activities (for children 3-5.9 years based on Adams 1993, pg 5A-3 of Exposures Factors Handbook), and also represents the average of 1 hour light activity and 1 hour of moderate activity for children ages 3-<10 years based on data from Layton 1993 (i.e., average of 0.5 m^3/hr for light activity and 1 m^3/hr for moderate activity, pg 5-16 Exposure Factors Handbook). In general, there is a paucity of ventilation data for children less than 6 years of age. One study reports ventilation rates for a 6 year old child average 0.83 m^3/hr for light activities (range 0.3 to 1.9 m^3/hr) and average 1.99 m^3/hr for moderate activities (range 1.7 to 2.6 m^3/hr), but determined these data were not appropriate to assess a 1-6 year old (pg 5A-7, of EFH). HED did not use the USEPA recommended inhalation rate of 1 m^3/hr for children (on page 5-24 of Exposure Factors Handbook) because this value is for children of all ages (infants to 18 years of age) and does not match the 15 kg child assessed in this analysis.
* The exposure time is assumed to be 2 hrs/day. This is based on the 95th percentile value (i.e., 121 minutes) for playing on grass for ages 1-4 years (Draft Residential SOPs December 18, 1997). This value could overestimate exposures for children that contact treated lawns less than 2

hours/day, but could underestimate exposures for children that play for more than 2 hours/day on treated lawns.

Table 13

Estimated Environmental Concentrations for Diazinon following Turf Treatment (MRID 44959101)

(Day of Treatment) (a)

Location	Average Turf Transferable Residue (TTR) (µg / cm²) (b)		Dislodgeable foliage residue (DFR) (Residue available for hand transfer from Grass) (µg / cm²) (c)	Soil Residue (µg/g) (d)	Air Concentrations (µg/sample) at 1.5 L/min (e)						Average Air Concentrations (µg/m³) (f)					
					Non-Irrigated			Irrigated			Non-Irrigated			Irrigated		
	non-irrigation	irrigation			0-2 Hr	2-4 Hr	0-4 Hr	0-2 Hr	2-4 Hr	0-4 Hr	0-2 Hr	2-4 Hr	0-4 Hr	0-2 Hr	2-4Hr	0-4 Hr
Liquid																
GA	0.0053	0.0032	2.2	30	0.092	0.077	0.084	0.071	0.069	0.07	0.509	0.428	0.469	0.394	0.383	0.389
CA	0.022	0.0049			1.02	0.36	0.691	0.296	0.077	0.187	5.652	2.055	3.836	1.644	0.428	1.039
PA	0.016	0.0033			0.87	0.275	0.573	0.188	0.213	0.2	4.836	1.535	3.178	1.044	1.183	1.11
Average	0.014	0.00382			0.66	0.237	0.449	0.185	0.12	0.152	3.66	1.34	2.49	1.03	0.665	0.85
Granular																
GA	0.0019	0.000664	2.5	33	ND (<0.1) (g)			ND (<0.1)(g)			ND (<0.578) (g)			ND (<0.578)		
CA	0.00072	0.000449			ND (<0.16) (g)			ND (<0.16) (g)			ND (<0.856) (g)			ND (<0.856)		
PA	0.0018	0.00132			0.109	0.264	0.187	ND (<0.138) (g)			0.606	1.466	1.036	ND (<0.138)		

Table 13
Estimated Environmental Concentrations for Diazinon following Turf Treatment (MRID 44959101)
(Day of Treatment) (a)

Location	Average Turf Transferable Residue (TTR) ($\mu g / cm^2$) (b)		Dislodgeable foliage residue (DFR) (Residue available for hand transfer from Grass) ($\mu g / cm^2$) (c)	Soil Residue ($\mu g/g$) (d)	Air Concentrations (μg/sample) at 1.5 L/min (e)						Average Air Concentrations ($\mu g/m^3$) (f)					
					Non-Irrigated			Irrigated			Non-Irrigated			Irrigated		
	non-irrigation	irrigation			0-2 Hr	2-4 Hr	0-4 Hr	0-2 Hr	2-4 Hr	0-4 Hr	0-2 Hr	2-4 Hr	0-4 Hr	0-2 Hr	2-4Hr	0-4 Hr
Average	0.0012	0.000812			0.079	0.131	0.105	ND (0.132) (g)			0.441	0.728	0.585	ND (<0.132) (g)		

(a) Application rate is based on the Registrant Study, MRID #449591-01, and the labels, Ortho® Diazinon Ultra™ (EPA Reg # 239-2643, Liquid water base concentrate, 22.4% ai, application rate = 4 lbs. ai/A), Ortho® Diazinon Soil and Turf ™ (EPA Reg # 239-2479, Granular, 4.84 % ai, application rate = 4.4 lbs. ai/A). Samples were taken from the plots during three sampling time intervals on the day of application (DAT-0) ; they were: Post-app, 4 hours, and then 8 hours.

(b) Turf transferable residue (TTR) is from a diazinon chemical specific (Novartis) Study (MRID #449591-01). The highest amount of residues were taken from the day of application (DAT-0), which appears to be within 1-4 hours after application, depending on the formulation. All liquid TTR values were collected immediately postapplication. The Granular TTR values were collected immediately postapplication for Georgia and 4 hours after application for California and Pennsylvania.

(c) Dislodgeable Foliar Residue (ug/cm2) = Application Rate (lb ai/A) * F (Fraction ai available or 0.05 as default) * 4.54E+8 ug/lb * 2.47E-8 A/cm2. It should be noted that the highest percentage of residues available from turf, of an application rate of 4 lbs. ai /A, treated with liquid formulated diazinon spray, was 0.05

% (California).

(d) Soil concentration (ug/g) = Application Rate (lb ai/A) * 1/cm * 4.54E+8 ug/lb * 2.47E-8 A/cm2 * 0.67 cm3/g soil.

(e) Airborne concentrations are based on a diazinon chemical specific (Novartis) Study (MRID #449591-01). Values represent the average of 4 samples per location from non-irrigated turf treatment over a 2-hour interval. The Registrant took samples for 8-hrs within the study on the day of application. Air concentrations adjusted for the low dose field fortification recoveries of 85.8% for Georgia, 58% for California and 64.7% for Pennsylvania.

(f) Air concentration ($\mu g/m^3$) = [[air sample from study (µg/sample)] / [1.5 L/min * 120 min]] * 1000 L/m^3

(g) Inhalation risks were not assessed because all air concentrations were non-detectable.

Crack and Crevice Treatment

The registrant has recently decided (July 2000) not to support indoor uses of diazinon. This includes use inside any structure or vehicle, vessel, or aircraft and/or on any contents therein, as noted previously in this document. The registrant submitted several studies that assessed residential post-application exposures. However, only one indoor study was of sufficient quality to use in risk assessment (MRID No. 443488-01). These studies are reviewed memo from J. Cruz to B. Chambliss and C. Eiden, March 15, 2000 (D229848, D240464, D246141, D261475).

Table 15, below, presents the daily indoor inhalation exposure results calculated using the results from the registrant-submitted study (MRID 44348801), which summarizes air monitoring data from several studies. According to these studies, the greatest potential for post application inhalation exposure to diazinon occurs during the 24 hours following the indoor application of diazinon. Based on the monitoring data from the three studies, at time 0 and 24 hours, an average indoor air concentration of 37.8 $\mu g/m^3$ was used as the indoor air concentration of diazinon during the first 24 hours after indoor application. The Agency default daily inhalation volume of 15.2 m^3/day for an adult was used to estimate the daily inhaled dose. Based on a 70 kg body weight, the daily inhaled dose of diazinon during the 24 hours following indoor application was calculated. The daily adult inhalation exposure-first 24 hours post application was 8.2 µg/kg/day. The daily toddler inhalation exposure-first 24 hours post application using 15 kg for body weight and 8.7 m^3/day inhalation volume (Agency default) was calculated to be 21.9 µg/kg/day.

Using the EPA's Non-occupational Pesticide Exposure Study (NOPES) Jacksonville summertime average indoor air concentration of 0.32 $\mu g/m^3$ (95^{th} percentile = 1.9 $\mu g/m^3$) , which represents a reasonable upper-bound estimate for this geographical area of diazinon air concentration after the initial application. The daily adult inhalation exposure was calculated to be 0.069 µg/kg/day and the daily toddler inhalation exposure was calculated to be 0.19 µg/kg/day.

The registrant did not address dermal exposure during this study. Data from several sources were examined to complete dermal exposure risk assessments. The data for dermal exposures were obtained from the following sources: the inhalation exposure data (lbs/gms ai applied) in this registrant's study, the current registrant's label- 4E's application rate, current real-estate information (e.g. room sizes within houses, built around 1961 to 1999), and other information (e.g. Tc, events/hr, surface area, etc.) from the Revised SOPs Residential Exposure Assessments Guide. **Table 16**, below, summarizes the dermal exposure, dose, and MOE estimates presented by HED.

Pet Collar Use

Several flea pet collar products are marketed containing diazinon as the active ingredient. HED has no chemical-specific data addressing the exposures of individuals from the use of pet flea collar products. In lieu of such data, it is necessary to estimate exposures from this scenario using HED's Residential SOP. The SOPs specify that in the absence of actual field data, "one percent (0.01) of the active ingredient applied to the pet be available for dermal exposure from handling flea collars. This assumption is based on the best professional judgement of the OPP/HED staff and assumed to be an upper-percentile value." Additionally, adults are assumed to weight 70 kg and infants and children were assumed to weigh 15 kg. The estimated exposures and MOEs for each typical pet collar products for adults and children are presented on **Table 17.**

(iii) Residential/Recreational Postapplication Risk Characterization

A summary of the postapplication risk is presented in **Table 14.** MOEs for residential/recreational postapplication exposures were derived by dividing the appropriate NOAEL or LOAEL, shown on **Table 2**, by the daily dermal, inhalation or oral exposure estimate. The target MOE is 100 for dermal and oral exposures and 300 for inhalation exposures, except intermediate-term dermal pet collar exposure, which has a target MOE of 300. MOEs below this level would represent a risk estimate of concern for the Agency. As noted previously, a short-term ARI was calculated because the dermal and inhalation target MOEs are different, there is a common dermal and inhalation toxicity endpoint (i.e., cholinesterase inhibition) and dermal, inhalation and oral exposures could occur simultaneously while a child plays on a treated lawn. For child exposures, oral exposure also contributed to the total MOE.

Lawn Treatment

Pathway-Specific Risk Estimates

For granular turf treatment, all adult and child residential postapplication risk estimates are greater than the target MOEs (i.e., 100 for dermal and oral and 300 for inhalation) and therefore do not exceed HED's level of concern, except for hand to mouth (MOE=3.8), granule ingestion (MOE= 0.26), and some child inhalation risk estimates from Pennsylvania. Child inhalation risk estimates based on air concentrations from non-irrigated treated turf in Pennsylvania are less than 300 for the 2-4 and 0-4 hour average air concentrations (MOEs of 190 and 270, respectively), and therefore, exceed HED's level of concern. However, no diazinon air residues were detected for granular-treated turf following irrigation, indicating that there are no inhalation risks if the lawn is irrigated (regardless of location). HED notes that diazinon was not detected in air samples in California or Georgia following granular turf treatment, and therefore, inhalation risks were not assessed.

For liquid turf treatment, all dermal and oral postapplication risk estimates are greater than 100, and therefore do not exceed HED's level of concern except the hand to mouth scenario (MOE=4.2). For non-irrigated treated turf, the inhalation MOEs for children are less than 300 (average MOE range from 76-210) depending on the time interval evaluated after turf treatment, while the adult inhalation MOE for 0-2 hour average concentration is also less than 300 (MOE=250), and therefore exceed HED's level of concern. As noted previously, the label does not require irrigation following turf treatment with a liquid formulation. Nevertheless, HED also evaluated the exposures and risks associated with irrigated liquid turf treatment to assist in risk management decisions. As shown on **Table 14**, with irrigation, most of the child inhalation MOEs (420-330) and all of the adult inhalation MOE (890-1400) are less than 300, and therefore, do not exceed HED's level of concern. The only irrigated MOE of concern is for children immediately after treatment (0-2 hour where MOE=270).

For inhalation, HED assessed a 0-2 hour time interval because it is possible that a child or adult could wander onto the treated turf before the turf has dried. HED also evaluated exposures and risks associated with 2-4 hour and 0-4 hour average air concentrations to provide a range of possible inhalation risk estimates that could result from turf treatment. It is likely that individuals will not be on turf treated with liquid formulations until after it has dried, which is usually 1-2 hours following application. There are uncertainties in the exposure assessments that could over- or under-estimate the risks. These uncertainties are discussed below following the presentation of aggregate risk estimates.

It is HED's policy to routinely conduct screening level assessments (based on standard values in the Residential SOPs) for children's incidental ingestion of granules when a granular pesticide may be applied in residential settings. The screening-level assessment for diazinon resulted in an MOE of 0.26 and is a risk of concern. Information on particle density (number of particles per pound or gram), carrier type (corn cob, clay), granular color, and average granular size is requested from the registrant in order to refine this screening level assessment.

<u>Aggregate Risk Estimates</u>

As noted previously for residential handlers, HED estimated total risk estimates using an aggregate risk index (ARI) because of different target MOE for dermal, oral (both MOE=100) and inhalation (MOE=300) exposure routes. The target ARI is $1 (i.e., ARIs less than 1 would exceed HED's level of concern).

For the child, total risk estimates are based on the combined exposure from dermal, non-dietary (hand-to-mouth, turf mouthing, soil ingestion), and inhalation in accordance with the ExpoSac policy (meeting minutes, October 5, 2000). Ingestion of granules is not included in the ARI because this exposure is considered to be episodic. For adults only dermal and inhalation risks were combined, since oral exposures to adults are considered insignificant.

As shown on **Table 14**, the ARIs for children are less than 1, and therefore exceed HED's level of concern for both liquid and granular turf treatment, regardless of whether the 0-2 or 2-4 hour average air concentrations are used to assess inhalation risks (ARI range from 0.03 to 0.04). The ARIs are similar for granular and liquid turf treatments, and are attributed primarily to the hand to mouth risk estimates. The ARIs for adults are greater than 1, and therefore do not exceed HED's level of concern, except for the liquid turf ARI using the 0-2 hour average air concentration (ARI=0.56). The ARI for children is conservative because it assumes a child is simultaneously conducting hand to mouth activities, ingesting soil and grass, dermally contacting the treated lawn and breathing diazinon residues in air the day of lawn treatment.

HED also evaluated aggregate dermal and inhalation exposures for children to evaluate the impact of excluding the oral pathways. As shown on **Table 14,** most dermal and inhalation ARIs for the liquid formulation also are mostly less than 1 (ARIs range from 0.2 to 1), and therefore, exceed HED's level of concern. However, the ARIs for non-irrigated granular turf treatment are mostly greater than 1 (ARIs range from 0.59 to 5), and therefore, do not exceed HED's level of concern. The exception is Pennsylvania, where the combined dermal and inhalation risks (for 2-4 hour average concentration) for a child result in an ARI of 0.59.

<u>Uncertainties</u>

As noted previously, all risk assessments involve the use of assumptions, judgement and available reliable data to varying degrees. Often, the available data are not the ideal data for evaluating potential exposure scenarios. This results in uncertainty in the numerical estimates of risk. Consideration of the uncertainty inherent in the risk assessment process permits better evaluation of the risk assessment and understanding of the possible human health impacts. Risks estimates may be overestimated or underestimated to varying degrees. The most important factors that contribute to the possible over-estimation of risk are:

(1) use of a 21 day inhalation toxicity endpoint based on whole body exposure in rats to assess a 2 hour exposure scenario;

(2) use of a 21 day rabbit dermal toxicity endpoint to assess a 2 hour exposure scenario;

(3) assumption that individuals contact treated turf for 2 hours the day of treatment (after the turf has dried for dermal and oral pathways), or inhale the volatilized residues immediately after treatment for inhalation (i.e., between 0-4 hours post application). ORETF survey data shows that 84% of the population waits at least 2 hours and 66% of the population waits at least 12 hours to enter treated turf;

(4) use of an inhalation rate of 0.7 m^3/hr for children less than 3 years of age, when there are few data available on this parameter;

(5) assuming that children play on treated lawns 2 hours the day of treatment, which could overestimate risks to children that are on treated lawns less than 2 hours. This value is based on the 95^{th} percentile value (i.e., 121 minutes) for playing on grass for ages 1-4 years (Draft Residential SOPs December 18, 1997); and

(6) use of one-half the detection limit for non-detectable residues in air measurements.

The most important factors that contribute to the possible under-estimation of risk are:

(1) This assessment does not assess potential exposures to all environmental metabolites, including diazoxon, which may form in the presence of chlorination (i.e., watering lawn with chlorinated water may enhance formation of diazoxon);

(2) The inhalation risk estimates are based on aerosol exposure only and do not account for possible vapor concentrations that could be present once the turf has dried (i.e., the registrant study did not provide vapor residue data beyond 2 hours postapplication, and these data have been requested from the registrant).

(3) Use of average air concentrations across three geographic locations, when two of the three locations (California and Pennsylvania) treated with the liquid formulations had higher average air levels (up to 1.5 times higher) four hours after turf treatment then the

geographic average;

(4) use of a child inhalation rate of 0.7 m^3/hr for children, which could underestimate exposure and risks to children 6 years of age and greater involved in moderate activities such as playing baseball, soccer, etc for more than 1 hour the day of treatment. There are data that report average inhalation rates for 6 year old children of 0.83 m^3/hr for light activities and 1.99 m^3/hr for moderate activities (p. 5A-7 of Exposure Factors Handbook, USEPA 1997); and

(5) assuming that children play on treated lawns 2 hours the day of treatment, which could underestimate risks to children that are on treated lawns more than 2 hours.

It should be noted that the diazinon air residues declined substantially (2-10 fold of initial air levels) within 8 hours of turf treatment for liquid formulation. In addition, the turf transferable residues dissipated rapidly over time, with residues non-detectable within 2 days postapplication. Therefore, the exposure and risk estimates on day 2 postapplication would be significantly less than the day of treatment exposure and risk estimates presented in this assessment.

In addition, the Residential SOPs are considered to be conservative scenarios for determining risk estimates. The adult and toddler transfer coefficients are based on the Jazzercise protocol and an upper percentile exposure duration value. The dermal exposure estimates, however, are more refined because they are based on actual TTR data compared to the incidental ingestion scenarios which are based on estimated grass and soil concentrations, and dislodgeable foliar residues (assuming that 5% of the application rate is transferable to a child's wet hand based on Clothier 1999).

Mitigation measures for residential exposure to diazinon residues may include the watering-in of both liquid and granular formulations on turf. There is some evidence from the Novartis study data submitted that watering increases the residue dissipation rate, and decreases the air concentrations. Turf labels require watering for granular formulations, but recommend watering prior to or following liquid turf treatment depending on the pest concern. This instruction, however, does not prevent contact with turf prior to watering-in.

Crack and Crevice Treatments

Inhalation exposure resulting from PCO'S indoor applications of diazinon based on US EPA's Screening Level Consumer Inhalation Exposure Software (SCIES) model and the Non-occupational Pesticide Exposure Study (NOPES). Based on the monitoring data from three monitoring studies, an average indoor air concentration of 38 : g/m^3 represents the indoor air concentration of diazinon during the first 24 hours after indoor application. The registrant assumes an inhalation absorption correction factor of 100 %. In this risk assessment (MRID No. 443488-01), the registrant also used a different inhalation NOAEL of 2.5 mg/kg/day from the acute oral study of Meyer, 1997 (the Agency's inhalation LOAEL is 0.026 mg/kg/day, for all time frequencies). The registrant's calculated inhalation dose for a body weight of 70kg, an average breathing volume of 15.2 m^3/day, and an average air concentration of 38 : g/m^3, is calculated as follows: [(15.2 m^3/day * 38 : g/m^3)/ 70kg] = 8.5 : g/kg/day for an adult. For a toddler, maximum inhalation exposure during the first 24 hours after application is calculated as follows: [(8.5 m^3/day * 38 : g/m^3)/ 15kg] = 22 : g/kg/day. Novartis estimates corresponding MOEs of 290 and 110 for adults and children, respectively (Target MOE=300). As shown on **Table 15,** HED estimated inhalation MOEs of 1.2 to 140 for children and 3.2 to 380 for adults based on an evaluation of registrant submitted study (MRID 44348801). All MOEs are of concern (i.e., less than 300), except for the adult MOE of 380 based on the mean data from the NOPES survey.

Dermal exposure was not assessed by the registrant. Therefore, HED estimated dermal exposures based on data from MRID 443488-01 and assumptions from the Draft Residential SOPs, and updated SOPs. As shown previously on **Table 16**, the dermal MOEs are less than 2 for both adults and children, and therefore exceed HED's level of concern (target MOE=100).

Pet Collar Use

As shown on **Table 17**, the intermediate and long-term dermal MOEs for children range from 66 to 120 and therefore, exceed HED's level of concern (target MOE of 300). The adult MOEs are greater than or equal to 300, for three collar products (MOEs range from 300 to 590), but are below 300 for one product (MOE=210). These risk estimates are considered high-end because they are based on screening methodology proposed in the Residential SOPs. Additional data on available transferable residues would help refine these exposure and risk estimates.

Table 14

Summary of Dose Estimates and Margins of Exposure for Postapplication Exposures on Treated Turf (Day of Treatment)

(MRID 44959101)

Scenario	**Time after Treatment**	**Central Tendency Dose (mg/kg/day)**				**Central Tendency MOE (Range) (a)**			
		Adult		**Child**		**Adult**		**Child**	
		non-irrigated	**irrigated**	**non-irrigated**	**irrigated**	**non-irrigated**	**irrigated**	**non-irrigated**	**irrigated**
Liquid Formulation									
Dermal	1-2 hour (when turf dry for non-irrigation); 4 hours (irrigation)	0.0058 (b)	0.0016 (b)	0.0097 (b)	0.0026 (b)	170 (110-460)	630 (490-750)	100 (66-270)	380 (290-450)
Hand to Mouth		NE		0.0598 (c)		NE		**4.2**	
Turf Mouthing (object to mouth)		NE		0.00187 (d)		NE		130	
Soil Ingestion		NE		0.0002 (e)		NE		1200	
Inhalation (f)	0-2 hr	0.0001	0.00003	0.00034	0.000096	**250** (**160**-1800)	890 (550-2300)	**76** (**49**-550)	**270** (**170**-710)
	2-4 hr	0.000038	0.000019	0.00012	0.000062	690 (460-2100)	1400 (770-2400)	**210** (**140**-650)	420 (**240**-730)

Table 14

Summary of Dose Estimates and Margins of Exposure for Postapplication Exposures on Treated Turf (Day of Treatment)

(MRID 44959101)

Scenario	Time after Treatment	Central Tendency Dose (mg/kg/day)				Central Tendency MOE (Range) (a)			
		Adult		Child		Adult		Child	
		non-irrigated	irrigated	non-irrigated	irrigated	non-irrigated	irrigated	non-irrigated	irrigated
	0-4 Hr	0.000071	0.000024	0.00023	0.000079	370 (**240**-1950)	1100 (820-2300)	**110** (**73**-600)	330 (**250**-720)
Total Aggregate Risk Index (ARI) (h)								**0.03 (0-2 hr inh) 0.04 (2-4 hr inh)**	**0.04 (0-2 and 2-4 hr inh)**
Dermal and Inhalation Aggregate Risk						**0.56 (0-2 hr inh)** 1 (2-4 hr inh)	1 (0-2 hr inh) 1.24 (2-4 hr inh)	**0.2 (0-2 hr inh) 0.42 (2-4 hr inh)**	**0.73 (0-2 hr inh)** 1 (2-4 hr inh)
Granular Formulation									

Table 14 Summary of Dose Estimates and Margins of Exposure for Postapplication Exposures on Treated Turf (Day of Treatment) (MRID 44959101)									
Scenario	**Time after Treatment**	**Central Tendency Dose (mg/kg/day)**				**Central Tendency MOE (Range) (a)**			
		Adult		**Child**		**Adult**		**Child**	
		non-irrigated	**irrigated**	**non-irrigated**	**irrigated**	**non-irrigated**	**irrigated**	**non-irrigated**	**irrigated**
Dermal	1-2 hour (when turf dry for non-irrigation); 4 hours (irrigation)	0.0005 (b)	0.0003 (b)	0.0009 (b)	0.0006 (b)	2000 (1300-3400)	3000 (1800-5400)	1200 (760-2000)	1800 (1100-3200)
Hand to Mouth		NE		0.066 (c)		NE		**3.8**	
Turf Mouthing (object to mouth)		NE		0.00206 (d)		NE		120	
Soil Ingestion		NE		0.00022 (e)		NE		1100	
Granule Ingestion		NE		0.97 (g)		NE		**0.26**	

Table 14
Summary of Dose Estimates and Margins of Exposure for Postapplication Exposures on Treated Turf (Day of Treatment)
(MRID 44959101)

Scenario	Time after Treatment	Central Tendency Dose (mg/kg/day)				Central Tendency MOE (Range) (a)			
		Adult		Child		Adult		Child	
		non-irrigated	irrigated	non-irrigated	irrigated	non-irrigated	irrigated	non-irrigated	irrigated
Inhalation (f)	0-2 hr	0.0000017 (PA)	Not detected (ND)	0.000057 (PA)	Not detected (ND)	1500-PA ND--CA and GA	Not detected (ND)	460–PA ND–CA and GA	Not detected (ND)
	2-4 hr	0.000042 (PA)		0.000136 (PA)		620--PA ND--CA and GA		**190**–PA ND–CA and GA	
	0-4 Hr	0.00003 (PA)		0.000096 (PA)		880--PA ND--CA and GA		**270**–PA ND–CA and GA	
Total Aggregate Risk Index (ARI) (h)								**0.04**	**0.04**

Table 14
Summary of Dose Estimates and Margins of Exposure for Postapplication Exposures on Treated Turf (Day of Treatment)
(MRID 44959101)

Scenario	Time after Treatment	Central Tendency Dose (mg/kg/day)				Central Tendency MOE (Range) (a)			
		Adult		Child		Adult		Child	
		non-irrigated	irrigated	non-irrigated	irrigated	non-irrigated	irrigated	non-irrigated	irrigated
Dermal and Inhalation Aggregate						5 (0-2 hr inh) 2 (2-4 hr inh) (PA only)	Not applicable (no inhalation risk)	1.3 (0-2 hr inh) **0.59** (2-4 hr inh) (PA only)	Not applicable (no inhalation risk)

ND=Non detect

(a) MOE = NOAEL / Exposure, where short-term dermal NOAEL is 1 mg/kg/day from a dermal study, the short-term oral NOAEL is 0.25 mg/kg/day from an oral toxicity study and the short-term inhalation LOAEL = 0.026 mg/kg/day from an inhalation study. Values represent an average of all data from the diazinon turf study, the range represents MOEs from the three different locations (CA, GA and PA) for which data are available. **Target MOE = 100 for dermal and oral and 300 for inhalation. Target ARI 1.**

(b) Dermal Dose (unabsorbed) (mg/kg/day) = TTR (µg/cm^2) * TC * 0.001 mg/ug * 2 hr/day / body weight, where adult and child body weights are 70 and 15 kg, respectively and TC are 14,500 and 5,200 cm^2/hr for adults and children, respectively.

(c) Hand-to-mouth (mg/kg/day) = DFR (µg/cm^2) * 20 events/hour * 20 cm^2/event * 0.5 (50% saliva extraction factor) * 2 hour/day * 0.001 mg/µg / 15 kg.

(d) Turf mouthing (mg/kg/day)=DFR (µg/cm^2)*25 cm^2 /day*0.5(50 % saliva extraction factor)*0.001mg/µg/15 kg

(e) Soil ingestion (mg/kg/day) = soil residue µg/g * 100 mg/day * 1x10-6 g/µg / 15 kg.

(f) Inhalation Dose (mg/kg/day) = [air concentration (µg/m3) * inhalation rate (m3/hr)*0.001 mg/µg * 2 hour] / body weight of 15 kg or 70 kg. Air concentration is the averag across geographic locations for liquid formulation. For granular formulation, only Pennsylvania was evaluated because air concentrations were non-detectable in Califor and Georgia for non-irrigated turf treatment. Adult inhalation rate is 1 m3/hr based on light activities USEPA p. 5-24 Exposure Factors Handbook. Child inhalation rate is 0.7 m3/hr based on play activities for 3-6 yr old children from Adams 1993, Exposure Factors Handbook pg. 5A-3, which is also the average of 1 hour light activities at 0.5 m3/hr and 1 hour of moderate activities based on data from Layton 1993, pg.5-16 for children 3-< 10 years. One-half non-detected value was used to assess exposure anc risk for some scenarios, in accordance with HED policy.

(g) Ingestion of granules (mg/kg/day) = 0.3 g/day * 0.0484 (% ai) * 1000 mg/g / 15 kg.

(h) Aggregate Risk index (ARI) = sum of oral, dermal and inhalation exposures, except for granule ingestion which is considered to be episodic for children, and sum of derm and inhalation for adults. ARI calculated based on both 0-2 hour and 2-4 hour inhalation MOEs.

Table 15
Post Application Diazinon Indoor House Inhalation Exposures

Source of Exposure Calculations	Air Concentration $\mu g/m^3$	Dose Daily Results mg/kg/day		MOEs[1]	
		Adult	Child	Adult	Child
24-Hour average postapplication value from Novartis 1980, 1981 and Wright and Leidy 1982	37.8 $\mu g/m^3$ (mean)	0.0082	0.022	3.2	1.2
NOPES -Daily Inhalation Exposure (for the mean and the 95th percentile)	0.32 (mean)	0.000069	0.00019	380	140
	1.9 (95th percentile)	0.00041	0.001	63	26

[1] = Margin Of Exposure (MOE) = Inhalation (for all time frequencies) LOAEL (0.026 mg/kg/day)/Daily Inhalation Dose. *The **Inhalation Target MOE = 300; which does not***

exceed HED's level of concern.

Table 16

Summary of Diazinon Indoor Post-application Short-Term Dermal Exposure Assessment Information

(Based on Novartis's post-application inhalation data)

Source (4E-Label) [1]	Application Rate		Area ($ft.^2$) (i)	Indoor Surface Residue ($\mu g/cm^2$) (l)	Dose (mg/kg/day) (m)		MOE (n)	
	Lbs.	gms.			Adult	Toddler	Adult	Toddler
EPA Reg# 100-463 @ 1%, 1.3 liters (a)	0.026	11.8	Kitchen 40.5 (j)	15.7 (hard surfaces)	15	25	0.068	0.04
EPA Reg# 100-463 @ 1%, 1.3 liters (b)	0.026	11.8	Kitchen 40.5 (j)	15.7 (o) (I0% skin contact of hard surfaces)	1.5	2.5	0.68	0.4
EPA Reg# 100-463 @ 0.5%, 1.3 liters (c)	0.013	5.9	Kitchen 40.5 (j)	7.8 (hard surfaces)	7.5	12	0.13	0.084
EPA Reg# 100-463 @ 0.5%, 1.3 liters (d)	0.013	5.9	Kitchen 40.5 (j)	7.8 (o) (I0% skin contact of hard surfaces)	0.75	1.2	1.3	0.8
EPA Reg# 100-463 @ 0.5%, 1-gal (e)	0.039	17.7	House 189 (k)	2.6 (carpet surfaces)	5	8.3	0.2	0.12
EPA Reg# 100-463 @ 0.5%, 1-gal (f)	0.039	17.7	House 189 (k)	2.6 (o) (25% skin contact of carpet surfaces)	1.2	2.1	0.84	0.48
EPA Reg# 100-463 @ 0.25%, 1-gal (g)	0.02	8.9	House 189 (k)	1.3 (carpet surfaces)	2.5	4.2	0.4	0.24

Table 16 Summary of Diazinon Indoor Post-application Short-Term Dermal Exposure Assessment Information (Based on Novartis's post-application inhalation data)								
Source (4E-Label) [1]	**Application Rate**		**Area (ft.^{2}) (i)**	**Indoor Surface Residue (µg/cm^2) (l)**	**Dose (mg/kg/day) (m)**		**MOE (n)**	
	Lbs.	**gms.**			**Adult**	**Toddler**	**Adult**	**Toddler**
EPA Reg# 100-463 @ 0.25%, 1-gal (h)	0.02	8.9	House 189 (k)	1.3 (o) (25% skin contact of carpet surfaces)	0.62	1	1.6	1

[1] = This label was used in the registrant's Study, MRID 443488-01.

(a) This concentration, and amount was approximately used in this study. The predominant area that was treated was in the kitchen (hard surfaces), and air sampling pumps were placed in the kitchen to collect the inhalation exposure data; therefore this dermal exposure/dose corresponds to the inhalation exposure recorded within this study report [see table 25 (a), above (Novartis-1980) for the corresponding average inhalation exposure from three studies (Novartis-1980, Novartis-1981, & North Carolina State University), and table 25(c), for their corresponding dose and MOE].

(b) The same information in foot note [a] above applies, except for assuming only 10 % dermal contact of hard surfaces with residents.

(C) The same information in foot note [a] above applies, except for the concentration; which has been reduced by half to 0.5%.

(d) The same information in foot note [a] above applies, except for assuming only 10 % dermal contact of hard surfaces with residents and the concentration; which has been reduced by half to 0.5%.

(e) This concentration and amount is typical for minor to moderate infestations of insects for an entire house's main living areas, see footnote 2[b], for details of which areas.

(f) This concentration and amount is typical for minor to moderate infestations of insects for an entire house's main living areas (see footnote 2[b], for details of which areas), except for assuming only 25 % dermal contact of carpet surfaces.

(g) This concentration and amount is typical for minor (pest free maintenance) infestations of insects for an entire house's carpeted main living areas (see footnote 2[b], for details of which areas).

(h) This concentration and amount is typical for minor (pest free maintenance) infestations of insects for an entire house's carpeted main living areas (see footnote 2[b], for details of which areas), except for assuming only 25 % dermal contact of treated carpet surfaces.

(i) The registrant's study, MRID # 443488-01, did not provide the square footage that was treated by the PCO in both North Carolina studies of 1980 & 1981; nor the area of the kitchens or houses where these studies took place.

(j) For Crack & Crevice application, the average square footage was obtained from real estate data of 6-7 houses, built in 1961 - 1999 and the treated base-board's footage. First, the average estimated potential treated perimeter was determined, for the kitchen; which is: Kitchen = 54 ft. [(14 x 2) + (13 X 2)]. And two, the estimated potential treated base-board footage was determined by assuming the base-board's height is 3.5 inches tall, 2 inches above it and then 3.5 inches out from the wall = 9 inches in all = 0.75ft. The total area treated of the kitchen was determined by taking the total linear feet by the estimated potential treated base-board's footage = 40.5 ft^2 .

(k) For Crack & Crevice application, the average square footage was obtained from real estate data of 6-7 houses, built in 1961 - 1999 and the treated base-board's footage. First, the average estimated potential treated perimeters were determined, and are as follows: Living Rm. = 60 ft. [(17 x 2) + (13 X 2)]; Dining Rm. = 44 ft. [(12 x 2) + (10 X 2)]; Master Bed Rm. = 54 ft. [(15 x 2) + (12 X 2)]; Bed Rm.-2 = 48 ft. [(13 x 2) + (11 X 2)]; and Bed Rm.-3 = 46 ft. [(13 x 2) + (10 X 2)] = total linear feet of 252. And two, the treated base-board footage was determined by the same method as in foot note 2[a]. The treated total area of the house was determined by taking the total linear feet by the estimated potential treated base-board's footage = 189 ft^2 .

Only the carpeted main living areas were considered; such as bed rooms, living rooms, and dining rooms, as a screening level to estimate what dermal exposures/does could be. Hallways, closets, basements, and utility areas were not considered at this time.

(l) Indoor Surface Residue (ISR-µg/cm^2) = [(lbs. ai / square footage area treated) X (50% of potential maximum ai concentration available from crack & crevice treatment) X (% of Indoor surface transferable residues- 5% for carpets, and - 10% for hard surfaces) X (Conversion factor- 4.54 X 10^8 µg/ lbs) X (Conversion Factor- 1.08 X 10^{-3} ft^2 / cm^2)].

(m) Dose = [ISR X (Conversion factor- 0.001 mg/µg) X (Transfer Coefficient-Tc, for adults = 16,700 cm^2/hr, and for toddlers = 6,000 cm^2/hr) X (Duration, for hard surfaces-4hours, and carpet surfaces-8hours)] / BW, for adults = 70 kg, and for toddlers = 15 kg.

(n) MOE = Short-term Dermal NOAEL (1 mg/kg/day) / Dermal Dose (mg/kg/day).

(O) For only 10% dermal contact of treated surfaces, reduce the Tc by 0.1. For only 25% dermal contact of treated surfaces, reduce the Tc by 0.25.

Table 26

Dermal Exposure and Risk Estimates from Diazinon Pet Collar Products

Product Registration	Weight of Flea Collar (g)	Percent Active Ingredient	Grams of Diazinon in Product	Total mg of Exposure (i.e., 1% of product)	Exposure (mg/kg/day) (a)		MOE (b) (Target 300)	
					Adult	Child	Adult	Child
EPA No. 2517-24	45	11	5	50	0.0048	0.022	210	45

Table 26 Dermal Exposure and Risk Estimates from Diazinon Pet Collar Products								
Product Registration	**Weight of Flea Collar (g)**	**Percent Active Ingredient**	**Grams of Diazinon in Product**	**Total mg of Exposure (i.e., 1% of product)**	**Exposure (mg/kg/day) (a)**		**MOE (b) (Target 300)**	
					Adult	**Child**	**Adult**	**Child**
EPA No. 2517-25	20	11	2.2	22	0.0021	0.0097	480	100
EPA No. 2517-29	12.2	15	1.8	18	0.0017	0.0081	590	120
EPA No. 2517-30	23	15	3.5	35	0.0033	0.015	300	66

(a) The Residential SOP were used (i.e., assumed 1% of the ai was available for dermal exposure) to estimate the total amount of diazinon available for exposure. Available residues were amortized over use time assuming linear dissipation. Exposure=total mg exposure / days of use / BW.

(b) MOE=NOAEL/exposure, where the NOAEL is 1 mg/kg/day from a 21-day dermal rabbit study. This endpoint was identified for intermediate and long-term dermal risk assessment with a **Target MOE=300**.

e. Summary of Postapplication Spray Drift/Track-In Risks

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method employed for diazinon. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with aerial as well as other application types where appropriate.

HED has concerns for the potential for children's exposure in the home as a result of agricultural and non-agricultural uses of diazinon. Environmental concentrations of diazinon in homes may result from spray drift, track-in, or from redistribution of residues brought home on the farmworker's clothing. Potential routes of exposure for children may include incidental ingestion and dermal contact with residues on carpets/hard surfaces.

There are limited data in literature that quantifies the levels of diazinon in household dust. These residues may persist indoors and the resulting exposures are of a potential chronic nature. It is not known at this time if the low levels in carpet dust would correspond to an absorbed dose in a child. The results from Bradman et al. (1997) are briefly discussed to illustrate concern that elevated diazinon residues maybe found in farm worker's homes. Bradman et al. (1997) monitored house dust in homes along with handwipe samples from children. The highest diazinon levels in house dust were found in farm worker residents. The results of the house dust are not reported here because the homes and surfaces monitored varied and contain small sample sizes. The values reported for diazinon residues on the farm worker's children's dominant hand (n=4, ages 1 to 2) are ND, 52, 125, and 220 ng. Readers are referred to the article for a more in-depth review.

The diazinon assessment reflects the Agency's current approaches for completing residential exposure assessments based on the guidance provided in the *Draft: Series 875-Occupational and Residential Exposure Test Guidelines, Group B-Postapplication Exposure Monitoring Test Guidelines*, the *Draft: Standard Operating Procedures (SOPs) for Residential Exposure Assessment*, and the *Overview of Issues Related to the Standard Operating Procedures for Residential Exposure Assessment* presented at the September 1999 meeting of the FIFRA Scientific Advisory Panel (SAP). The Agency is, however, currently in the process of revising its guidance for completing these types of assessments. Further research into children's exposures resulting from agricultural uses of pesticides are being conducted by the Agency's Office of Research and Development through the STAR (Science to Achieve Results) grant program. The STAR program can be accessed at ***http://es.epa.gov/ncerqa/grants/*** Modifications to this assessment shall be incorporated as updated guidance becomes available. This will include expanding the scope of the residential exposure assessments by developing guidance for characterizing exposures from other sources already not addressed such as from spray drift; residential residue track-in; and exposures to farm worker children.

5. Aggregate Exposure and Risk Characterization

When target MOEs for multiple exposure pathways differ, but exposures across those pathways must be combined under an aggregate risk assessment, HED uses the Aggregate Risk Index method (ARI method). ARIs greater than 1.0 do not exceed HED's level of concern. Results of the specific aggregate risk assessments included in this document are provided below.

Acute Aggregate Risk Estimates

The aggregate risk assessment for acute exposures to diazinon includes one day exposures through food and drinking water, only. Exposure to diazinon from food sources (based on refined exposure estimates) and drinking water (based on surface and groundwater monitoring data and groundwater model estimates) do not exceed HED's level of concern for acute dietary risk for any subgroup analyzed. However, if surface water *model* estimates are used in the assessment, risk estimates for all population subgroups exceed HED's level of concern.

Given the uncertainty in the model and monitoring estimates relative to each other (greater than 20x) for surface water concentrations of diazinon, and therefore, the uncertainty relative to diazinon concentrations in actual drinking water, HED recommends that the acute exposures to diazinon in drinking water, and subsequently acute aggregate exposure, be reassessed once sufficient surface-water sourced drinking water monitoring data on diazinon and its toxic degradates become available for use.

Short-term Aggregate Risk

HED has concerns for aggregate short-term exposures to diazinon for residential handlers of lawn products. Risk estimates for handlers for combined dermal and inhalation exposures to diazinon from granular and liquid formulations used to treat lawns exceed HED's level of concern. HED also has concerns for short-term postapplication exposures to diazinon for adults and children in the home after indoor crack and crevice treatments and outside the home after liquid or granular lawn treatment.

Short-term aggregate risk assessments combine short-term residential exposures with average, dietary (food and drinking water) exposures. However, because all ARIs for exposures of residential handlers are below 1, and therefore exceed the Agency's level of concern, HED has not aggregated short-term exposures from food, drinking water and residential exposures. Aggregating additional exposures from food and drinking water with these residential exposures would only result in a risk estimate that would further exceed HED's level of concern. Until residential short-term dermal exposures can be mitigated for residential handlers, aggregate short-term risk estimates exceed HED's levels of concern.

Postapplication dermal and inhalation exposures to children from indoor (crack and crevice) and outdoor (lawn) treatments result in ARIs less than 1. Therefore, HED has not aggregated short-term exposures from food and drinking water with postapplication residential exposures. Aggregating additional exposures from food and drinking water with these residential exposures would only result in a risk estimate that would further exceed HED's level of concern. Until postapplication residential short-term exposures can be mitigated, aggregate short-term risk estimates for postapplication exposures to diazinon exceed HED's levels of concern.

Chronic Aggregate Risk

The chronic aggregate risk assessment for exposures to diazinon includes long-term, average exposures to diazinon through food and drinking. There are no residential uses that result in chronic exposure. Therefore, chronic aggregate risk estimates based on estimated exposures from food and groundwater are the same as those presented under the section on chronic drinking water risk estimates. HED concludes chronic aggregate exposures to diazinon in food and ground-water sourced drinking water do not exceed levels of concern.

Chronic aggregate risk estimates based on estimated exposures from food (based on refined exposure estimates) and surface water (based on ambient monitoring data) do not exceed HED's level of concern for chronic aggregate exposures to diazinon in food and surface-water sourced drinking water. However, *model* estimates for concentrations of diazinon in surface water indicate there is a potential concern for all population subgroups analyzed However, given the uncertainty in the model and monitoring estimates relative to each other (almost 20x) for surface water concentrations of diazinon, and therefore, the uncertainty relative to long-term concentrations of diazinon in actual drinking water, HED recommends that the chronic exposures to diazinon in drinking water, and subsequently chronic aggregate exposure, be reassessed once sufficient surface-water sourced drinking water monitoring data on diazinon and its toxic degradates become available for use.

6. Cumulative Risk Assessment

Cumulative risk will be addressed once OPP has finalized its' policies and procedures for conducting a cumulative risk assessment for organophosphates. This is an ongoing effort in OPP.

7. Data Requirements

The following data are required at this time:

Toxicology - The HIARC has determined that a 90-day repeated dose dermal toxicity study in rats be performed to support the conclusions from the 21-day dermal toxicity study in rabbits.

Product Chemistry - All pertinent generic data requirements are satisfied for the Novartis and Makhteshim "unstabilized" TGAIs, except that data pertaining to stability (OPPTS 830.6313) are outstanding for the Makhteshim TGAI and data concerning UV/visible absorption for the PAI (OPPTS 830.7050) are required for both TGAIs. All pertinent product-specific data requirements are satisfied for the Novartis 87% FI. Additional product-specific product chemistry data are required for the Prentiss 80%, 50%, 48.7%, 25%, and 10% FIs; the AgrEvo 10% and 5% FIs; and the Makhteshim 92% and 87% FIs. No product chemistry data have been submitted in support of reregistration of the Sureco 70.31%, 25%, and 12.5% FIs and the AgrEvo 25% FI. Data requirements for the repackaged Gowan and Drexel 87% FIs will be satisfied by data for the source products. The product chemistry data requirements for diazinon products are presented in the attached summary tables in the Residue Chemistry Chapter for diazinon. Refer to these tables for a listing of the outstanding product chemistry data requirements.

Residue Chemistry - Additional residue data are required for beans (lima), blueberries, celery, cucumbers, hops, dried peas (IR-4), spinach, sugar beets, and Swiss chard. Additional residue data on sugar beets reflecting current label rates and PHI are necessary to determine if feed additive tolerances are necessary. Registrant agreed to provide additional data on representative crops from limited rotational crop studies.

Occupational Exposure - Handler and postapplication data requirements will be determined based on risk mitigation meetings with the registrant and growers. There are no chemical specific exposure data for diazinon sheep treatments and mushroom houses; therefore the Agency is requiring data and/or further clarification of the use patterns.

Mushroom houses: No data were submitted in support of postapplication exposures for workers re-entering mushroom houses. EPA has identified potential dermal and inhalation exposures resulting from this indoor application. The Diazinon 50W label (EPA Reg. No. 100-460) directions for mushroom houses is to use a spray dilution rate of 0.04 to 0.05 lb ai/gallon and apply "on outside and inside walls, floors and sideboards of mushroom houses after compost has been pasteurized by heating ... and spray over the plastic covering the beds and trays after spawning." Potential dermal exposures in mushroom houses may arise from workers contacting treated surfaces as all surfaces may be treated. The potential inhalation exposures may result from air concentrations of diazinon in the mushroom house resulting from the application before or after ventilation. Additional data are needed to estimate the potential for dermal exposure in mushroom houses including (1) identification of mushroom house activities that may result in dermal contact, (2) the residue levels on the sideboards and plastic covering the beds and trays, and (3) direct dermal exposure measurements or transfer coefficients. Additional data are also needed to determine air concentrations of diazinon over time. In lieu of air concentration data to calculate exposure/risk, HED determined an allowable air concentration based on the inhalation LOAEL of 0.1 mg/m3 from a 21-day whole body aerosol study exposing rats 6-hours per day and the uncertainty factor of 300. The estimated 6 hour time-weighted-average (TWA) allowable air concentration is 0.0003 mg/m3 (i.e., LOAEL of 0.1 mg/m3 divided by 300 UF). This calculation assumes that the rat and human activity level for a breathing weight is equivalent.   The LOD from the air sampling portion of the diazinon lawn treatment study (MRID 449591-01) is listed as 0.0006 mg/m3 (see study results in this chapter for actual air concentration levels at specific time intervals).